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The BULLETIN

American Society of Hospital Pharmacists

MEMBERSHIP in the American Society of Hospital Pharmacists and the American Pharmaceutical Association is open to all practicing Hospital Pharmacists. With membership is included subscriptions to THE BULLETIN of the American Society of Hospital Pharmacists and to the two *Journals* of the American Pharmaceutical Association, as well as the several services of both organizations.

ADVERTISING will be accepted, subject to editorial approval, for prescription products as well as for other items used extensively in hospitals. Inquiries should be sent to the Associate Editor of THE BULLETIN, 1020 Ferdon Road, Ann Arbor, Mich.

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The American Society of Hospital Pharmacists, an affiliate of the American Pharmaceutical Association, is a national organization devoted to the profession of hospital pharmacy and dedicated to the improvement of pharmaceutical service in the interest of better patient care in hospitals.

IN THIS ISSUE

THE BULLETIN is published bimonthly at Hamilton, Illinois, by the American Society of Hospital Pharmacists in cooperation with the Division of Hospital Pharmacy of the American Pharmaceutical Association. Editorial office at 1313 East Ann Street, Ann Arbor, Mich. Entered as second class matter July 19, 1951 at the post office at Hamilton, Illinois. CONTRIBUTIONS will be accepted if they are of general interest to those in hospital pharmacy. The editors reserve the right to revise all material submitted, if necessary. The American Society of Hospital Pharmacists and the American Pharmaceutical Association assume no responsibility for the statements and opinions advanced by contributors to THE BULLETIN. Views expressed in the editorials are those of the editor and do not necessarily represent the official position of either the American Society of Hospital Pharmacists or the American Pharmaceutical Association.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

The following monographs and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of THE BULLETIN include those published in the *Journal* to October 1, 1957.

NOTICE

New and Nonofficial Remedies 1957 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1957 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 1956. The index listed below contains those drugs evaluated and published between October 1, 1956 and October 1, 1957.

INDEX TO EVALUATED DRUGS, THIS ISSUE

INDEX TO EVALUATED DRUGS PUBLISHED IN THE JANUARY-FEBRUARY, MARCH-APRIL, MAY-JUNE, JULY-AUGUST, AND SEPTEMBER-OCTOBER ISSUES OF THE BULLETIN.

Notice of Change in Operation

Listing of Preparations with Monographs

As an aid to physicians in writing prescriptions, the Council has adopted an expansion of the section in New and Nonofficial Drugs, "Principles Governing the Evaluation of Drugs Described in New and Nonofficial Drugs," to provide for listing pharmaceutical preparations, including either sizes or strengths, in conjunction with monographs published in the Council's column of *The Journal* and in future annual editions of New and Nonofficial Drugs. Available dosage forms, and either sizes or strengths, will be listed alphabetically according to appropriate nonproprietary pharmaceutical terminology only. In order to avoid undue expansion of monographs, with this kind of information, available sizes or strengths will be limited to dosage units or concentrations, depending on the type of formulation.

The listing of available preparations, which is instituted with this issue of *The Journal,* should not be construed as affecting any statements in monographs that may be critical of the usefulness, safety, suggested dosage, concentration, or particular route of administration of a drug. However, it is hoped that this added feature will increase the usefulness of the Council's publication to physicians when such information is desired for prescribing.

The Council will continue to list applicable commercial names of evaluated drugs of which it is informed and urges the continued cooperation of industry in supplying scientific data and reports of investigations to aid in the early evaluation of new drugs. Commercial outlets are further invited to supplement such future data with information on available dosage forms, sizes, and strengths or otherwise to inform the Council respecting any additions or corrections concerning preparations which are included in subsequently published monographs. The Council also desires information concerning adverse reactions to drugs that may appear after extensive use.

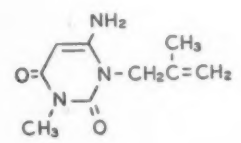
This notice of the desire of the Council to include dosage preparations and to continue its policy for listing commercial names will not be repeated in the Council's column of *The Journal* since statements to this effect will appear annually in New and Nonofficial Drugs.

J. Am. Med. Assoc. 165:155 (Sept. 14) 1957.

Amisometradine

Rolicton®

Amisometradine is 1-methallyl-3-methyl-6-aminotetrahydropyrimidinedione.—The structural formula of amisometradine may be represented as follows:



Actions and Uses

Amisometradine, an orally effective, nonmercurial diuretic agent, is a structural isomer of aminometradine, and it pharmacological actions are similar to those of the latter agent. Thus, amisometradine is proposed for

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the maintenance of an edema-free state in patients responsive to diuretic therapy and for the initiation of diuresis in most edematous conditions except severe congestive heart failure. The drug also may reduce or, in mild cases, eliminate the need for parenteral injections of mercurial diuretics. Amisometradine has been successful'y employed for the gradual mobilization of edema fluid in a substantial number of patients with mild to moderate congestive heart failure, hepatic cirrhosis, and the nephrotic syndrome. It has also been useful for the management of water and electrolyte retention during pregnancy (mild preeclampsia) and in the premenstrual period.

The chief difference between amisometradine and aminometradine lies in the possibly diminished incidence of gastrointestinal upsets associated with the former drug. Some data have indicated that whereas nausea or vomiting occur in approximately 20 to 30% of patients to whom aminometradine is administered, this incidence is reduced to about half, or 10 to 15%, when amisometradine is employed. Thus, from the standpoint of patient tolerance, amisometradine appears to offer some advantage. Since the clinical effectiveness of both drugs appears to be about the same, it seems likely that amisometradine may eventually replace aminometradine for the treatment of edema.

Amisometradine has not been extensively studied from the standpoint of serious toxic effects, and although the drug so far has not been observed to cause such reactions, physicians should be alert to the possibility of their occurrence with extensive and prolonged use.

Dosage

Amisometradine is administered orally. Dosage is governed largely by severity of edema and individual response as reflected by the serial weight record of the patient. As a general guide, 400 mg. may be administered four times daily with meals on the first day of therapy and twice daily thereafter. Patients with mild edema may be satisfactorily maintained on 400 mg. or less per day. On the other hand, daily amounts up to 3.2 Gm. may be required in more severe cases.

Preparations: tablets 400 mg.
Applicable commercial name: Rolicton.
G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of amisometradine.
***J. Am. Med. Assoc.* 165:155 (Sept. 14) 1957.**

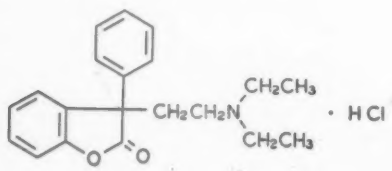
Preparations

Tablets Amisometradine (Rolicton) 0.4 Gm.

Amolanone Hydrochloride

Amethone® Hydrochloride

AMOLANONE HYDROCHLORIDE is 3-(β-diethylaminoethyl)-3-phenyl-2-benzofuranone hydrochloride. — The structural formula of amolanone hydrochloride may be represented as follows:



Actions and Uses

Amolanone hydrochloride is a benzofuranone derivative with both anticholinergic and local anesthetic actions. The drug formerly was used as an intramuscularly administered antispasmodic for the relief of ureteral colic due to calculi, spasm, and instrumentation, a purpose for which it has been withdrawn. Its clinical use is now confined exclusively to topical anesthesia of the lower urinary tract. When it is instilled into the urethra, anesthetic effects are stated to become apparent within 5 minutes and to persist for 15 to 30 minutes. Accordingly, the drug is proposed for the production of topical anesthesia prior to carrying out such urologic procedures as catheterization, urethral dilatation, cystoscopy, and panendoscopy. It is also proposed for the relief of pain in such conditions as interstitial cystitis with ulceration (Hunner's ulcer). However, because some investigators report unsatisfactory results with this agent, it is difficult to define with certainty the real usefulness of amolanone hydrochloride as a topical anesthetic. Some urologists indicate that the drug is equal or superior to butacaine and procaine; a minority has been unable to produce satisfactory anesthesia. Hence, the ultimate usefulness of this drug as a local anesthetic must await the results of further clinical experience.

On the basis of prior experience with the drug as a systemic spasmolytic and more recent reports on its use as a topical anesthetic, amolanone hydrochloride may be described as a drug of low toxicity. After intraurethral instillation, only isolated instances of slight giddiness, a transitory burning sensation, or mild dizziness have been reported. There is no evidence that appreciable quantities of the drug are absorbed from the urethral mucosa, and it has been used in patients with lower urinary tract bleeding without untoward effects. In view of its apparently low order of toxicity and the favorable reports so far recorded, further careful trial of the local anesthetic action of this drug is indicated.

Dosage

Amolanone hydrochloride is employed as a 0.33% solution (3.3 mg. per cubic centimeter) for intraurethral instillation prior to performing urologic precedures. This solution should not be injected into the tissues. The urethra is filled with the solution and the meatus is closed with a penile clamp. After three to five minutes, the clamp is removed and the procedure begun.

Applicable commercial name: Amethone Hydrochloride.
Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of amolanone hydrochloride.
***J. Am. Med. Assoc.* 164:1755 (Aug. 17) 1957.**

Preparations

Injection Amolanone (Amethone) Hydrochloride 9 percent; 20 ml. vials.

Ethchlorvynol — Use for Daytime Sedation

The Council has evaluated the use of ethchlorvynol (Placidyl) for daytime sedation. This nonbarbiturate hypnotic has previously been described as useful for the induction of sleep in selected patients with simple insomnia. (See the monograph on ethchlorvynol in New and Nonofficial Remedies.) On the basis of additional evidence, the Council concluded that the drug may also be given in small doses during the day to allay or calm certain patients with organic or functional disorders characterized by anxiety or tension. Its

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ADRESTAT (F) — *1-cc ampuls, each containing:*
5 mg Adrenochrome Semicarbazone (present as Carbazochrome Salicylate, 130.0 mg)*
Boxes of five 1-cc ampuls

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*Pat. Nos. 2,581,850; 2,506,294

clinical employment for this purpose has been confined largely to patients with mild anxiety neuroses, hypertension, and various skin diseases. It has also been used on a limited scale in patients with asthma, peptic ulcer, and cardiac disorders. Currently available evidence indicates that the drug exerts a mild sedative effect in such patients and that the incidence of side-effects is low (about 8%). Side-effects so far encountered include drowsiness, fatigue, hang-over, ataxia, vertigo, headache, nightmares, mental confusion, bad after-taste, nausea, and vomiting. There has been no observed tendency toward development of psychic dependence or habituation. Pending the accumulation of more clinical information, however, this possibility should be kept in mind, particularly when the drug is used over prolonged periods of time.

Dosage of ethchlorvynol for use as a daytime sedative should be individualized according to the response of the particular patient. Oral dosage usually ranges from 100 mg. twice daily to 200 mg. three times a day. If the drug appears to be rapidly absorbed, producing transient giddiness or ataxia, these side-effects will be minimized if the medication is given with a glass of milk or other light refreshment.

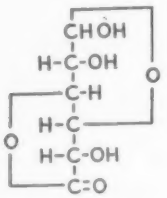
The Council voted to expand the monograph in New and Nonofficial Drugs to describe the use of ethchlorvynol as a daytime sedative.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of this additional use of ethchlorvynol.

J. Am. Med. Assoc. 165:157 (Sept. 14) 1957.

Glucurolactone — Glucurone®

GLUCUROLACTONE is the γ-lactone of D-glucofuranuronic acid.—The structural formula of glucurolactone may be represented as follows:



Actions and Uses

Glucurolactone is the gamma lactone of glucuronic acid, an important body constituent that is believed to possess at least two significant metabolic functions. It is an essential unit of tissue structure, comprising part of the composition of connective tissue and collagen, particularly of cartilage, periosteum, nerve sheath, joint capsule, tendon, and synovial fluid. It also occurs in intercellular cement substance and in blood vessel walls. Glucuronic acid is of additional metabolic importance as a detoxifying agent, combining with many foreign and deleterious substances that are then excreted in the urine as innocuous glucuronic acid conjugates.

As a physiological body constituent, glucuronic acid and its more stable lactone have been considered possible therapeutic agents in several disease entities. Although they were previously suggested for a variety of purposes, clinical experience has centered principally about the use of these compounds in the treatment of arthritis, rheumatism, and associated collagen diseases. It has been surmised that the destruction of bone and cartilage, which characterizes these conditions, may result from a deficiency of glucuronic acid required for normal metabolism and that such deficiency may also involve the cement substance affected in the collagen diseases. It has also been surmised that patients in this category may suffer from a defect in detoxicating mechanism as indicated by excessive toxicity from focal and other infections. Although there is no valid evidence to support this view, glucurolactone has been proposed for use in arthritic conditions as an orally given absorbable, stable form of glucuronic acid to restore and maintain metabolic balance in fibrous tissue and to help meet daily detoxicating requirements. Although some observers believe that the drug exerts a beneficial clinical effect, the number of patients in which such results have been reported is too small to permit any positive conclusion. Since the presently available evidence is largely from uncontrolled studies, it is also difficult to determine whether the favorable responses thus far reported were due to the action of the drug or to spontaneous remissions so characteristic of this group of diseases. Thus, while there may be some hypothetical reasons for the use of glucurolactone for the treatment of joint and collagen diseases, a definite statement regarding its usefulness must await the results of better controlled, long-term clinical studies.

Unlike free glucuronic acid or its salts, glucurolactone is readily absorbed from the gastrointestinal tract. It is apparently broken down to free glucuronic acid in the body, since detectable increases in this constituent may be found in the blood and urine after the oral administration of its lactone. Both laboratory and clinical experience indicates glucurolactone to be a relatively nontoxic substance. In humans, prolonged administration has not been accompanied by any manifestations of serious deleterious effects. Occasionally, flushing of the face and mild gastrointestinal distress have been observed. These effects usually subside with a reduction in dosage or with temporary withdrawal of the drug.

Dosage

Glucurolactone is administered orally. In the treatment of joint and arthritic-like conditions, the daily administration of 2 Gm. of glucurolactone in four divided doses should be considered experimental. If the drug is employed at all, administration for one month or more may be required before any therapeutic results are apparent. Should a favorable effect be obtained, maintenance dosage and duration of subsequent therapy should be governed by individual response. The trial of glucurolactone in arthritic patients does not obviate the need for more important and better established therapeutic measures.

Applicable commercial name: Glucurone.

Reed & Carnick cooperated by furnishing scientific data to aid in the evaluation of glucurolactone.

J. Am. Med. Assoc. 164:2046 (Aug. 31) 1957.

Preparations

Tablets Glucurolactone (Glucurone) 0.5 Gm.

Hexocyclium Methylsulfate — Tral®

HEXOCYCLIUM METHYLSULFATE is N-(β-cyclohexyl-β-hydroxy-β-phenylethyl)-N′-methylpiperazine dimethylsulfate.—The structural formula of hexocyclium methylsulfate may be represented as follows:

a new recourse
for severe
bacterial infections--
even when other
antimicrobials fail

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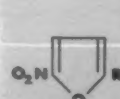
FURADANTIN I.V. solution is dissolved aseptically in a sterile diluent at room temperature, just prior to use by intravenous drip only. Full dosage instructions and discussion of indications and side effects are enclosed in each package. FURADANTIN I.V. is now available to all hospital pharmacies.



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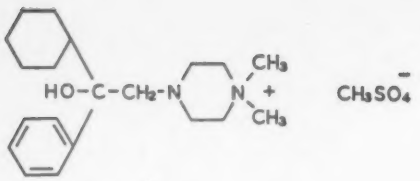
neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK



Actions and Uses

Hexocyclium methylsulfate, a synthetic anticholinergic quaternary ammonium compound, is chemically related to certain other drugs of this class and is qualitatively similar to these drugs in pharmacological action. After therapeutic doses have been administered, the autonomic blocking effects of hexocyclium methylsulfate are limited to effector cells innervated by postganglionic cholinergic nerves. At sufficient doses, in animal experiments, the drug inhibits gastrointestinal motility and spasm, diminishes gastric secretion, dilates the pupil, inhibits salivation, relaxes the musculature of the bladder, and counteracts the muscarinic effect of choline esters. In these respects, its principal pharmacological actions as well as side-effects may therefore be described as atropine-like. On a weight basis, the drug is less potent than atropine in vitro but is more potent by a number of tests in vivo. In large doses in animals, hexocyclium methylsulfate (and other compounds of its class) produces ganglionic blockade and curare-like effects interfering with neuromuscular transmission. The metabolic fate and excretion of hexocyclium methylsulfate are not known. The drug is readily absorbed from the gastrointestinal tract. Its onset of action is prompt, and, after ordinary doses, anticholinergic effects persist about three to four hours. No apparent cumulative toxic effect in animals has been observed after prolonged administration of large daily doses.

Hexocyclium methylsulfate may be used for the adjunctive management of peptic ulcer and other gastrointestinal disorders associated with hyperacidity, hypermotility, and spasm in which anticholinergic action might be considered beneficial. The antisecretory response to a fixed dose of hexocyclium methylsulfate appears to be variable. In some patients, gastric secretion is reduced to the point of anacidity; in others, the response is less marked or is minimal. The latter might be attributed to insufficient dosage. For the control of functional disorders of the gastrointestinal tract, especially peptic ulcer, hexocyclium methylsulfate should not be employed to the exclusion of dietary restriction and the use of antacids and sedatives. In certain cases, these measures may be more important in the therapeutic regimen than anticholinergic drugs. In some cases, anticholinergic drugs are not indicated or are without benefit. Although hexocyclium methylsulfate effectively allays hypermotility and hyperacidity, there is no evidence that it possesses greater therapeutic effectiveness than certain other drugs of this class.

Side-effects associated with hexocyclium methylsulfate are those of anticholinergic drugs in general. Dryness of the mouth (xerostomia) may be encountered when therapeutically effective doses are administered, but it is often transient and is usually mild. Likewise, blurring of vision, difficulty in urination, and palpitation may occur but usually only with excessive doses. Side-effects can often be minimized by adjustment of dosage. As with any new drug, until more experience is gained, physicians should be alert to the possible development of serious untoward effects that may result from continued use of the drug.

Dosage

The suggested initial dosage for adults is 25 mg. four times daily, administered orally, preferably before meals and at bedtime. The maintenance dosage of hexocyclium methylsulfate should be arrived at by careful adjustment to the needs and tolerance of the individual patient.

Applicable commercial name: Tral.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of hexocyclium methylsulfate.

J. Am. Med. Assoc. 164:1756 (Aug. 17) 1957.

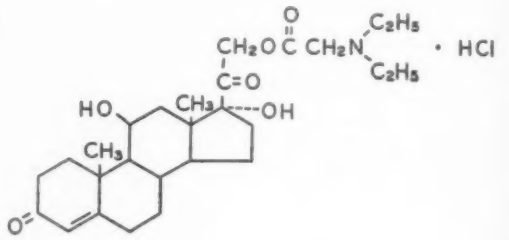
Preparations

Tablets Hexocyclium (Tral) Methylsulfate 25 mg.
Tablets Hexocyclium (Tral) Methylsulfate 25 mg. with Phenobarbital 15 mg.

Hydrocortamate Hydrochloride

Magnacort® Hydrochloride

HYDROCORTAMATE HYDROCHLORIDE is 17-hydroxycorticosterone-21-diethylaminoacetate hydrochloride. — The structural formula of hydrocortamate hydrochloride may be represented as follows:



Actions and Uses

Hydrocortamate hydrochloride, an ester-salt of hydrocortisone, is used for the treatment of dermatoses known to be responsive to topical gluco-corticoid therapy. The drug exerts an excellent anti-inflammatory action against such cutaneous eruptions and is believed to be approximately twice as potent, milligram for milligram, as free hydrocortisone or it acetate ester. Thus hydrocortamate hydrochloride is effective against acute or chronic dermatoses that have an allergic or inflammatory basis and are associated with pruritus. These would include, among others, such conditions as atopic and contact dermatitis, pruritus with lichenification, seborrheic dermatitis, and nonspecific anogenital pruritus. Clinical experience to date has been confined largely to short-term therapy on relatively limited areas of the body. Although the possibility of systemic reaction after prolonged or intensive therapy does exist, this appears to be quite unlikely. To date, no reactions suggestive of systemic absorption have been observed with hydrocortamate hydrochloride or with any other topical preparation of hydrocortisone. Likewise, no appreciable changes in eosinophil counts or excretion of 17-ketosteroids have been demonstrated after such therapy. Nevertheless, pending the accumulation of more information on this subject, hydrocortamate hydrochloride should be used cautiously in long-term therapy, especially in cases in which large areas of abnormal skin surface are involved. The drug should not be applied to infected areas. Its sensitizing potential is not known, but, in view of its similarity to other local preparations of this class, this is considered to be negligible. The ointment base rather than the drug may elicit some sensitization in particular instances.

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Dosage

Hydrocortamate hydrochloride is applied topically in a 0.5% ointment (5 mg. per gram). A small quantity should be applied to the affected areas of skin two or three times daily.

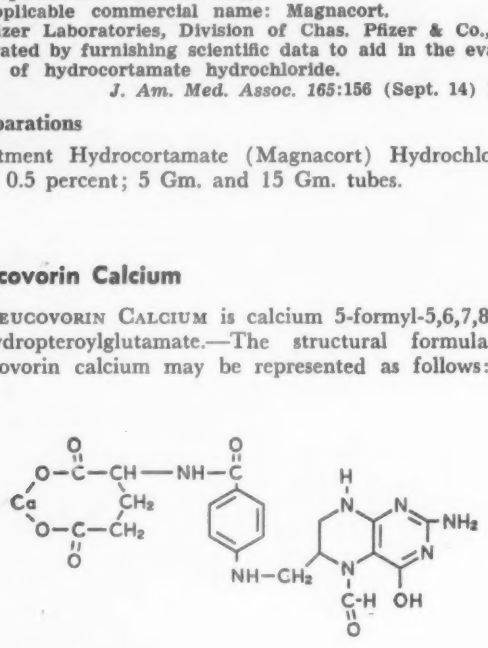
Preparations: ointment 0.5%.
Applicable commercial name: Magnacort.
Pfizer Laboratories, Division of Chas. Pfizer & Co., cooperated by furnishing scientific data to aid in the evaluation of hydrocortamate hydrochloride.
***J. Am. Med. Assoc.* 165:156 (Sept. 14) 1957.**

Preparations

Ointment Hydrocortamate (Magnacort) Hydrochloride 0.5 percent; 5 Gm. and 15 Gm. tubes.

Leucovorin Calcium

LEUCOVORIN CALCIUM is calcium 5-formyl-5,6,7,8-tetrahydropteroylglutamate.—The structural formula of leucovorin calcium may be represented as follows:



Actions and Uses

Leucovorin calcium, the calcium salt of the active metabolite of folic acid, is utilized for growth of the bacterial species Leuconostoc citrovorum. Hence, leucovorin is frequently referred to as citrovorum factor or, less commonly, folic acid. In man and animals, folic acid per se is metabolically inactive; it must be converted to leucovorin in the tissues in order to exert a stimulating effect on the proliferation of all blood cellular elements. If this conversion is blocked, as with the folic acid antagonists aminopterin or A-methopterin, hematopoiesis is depressed. This is, of course, the therapeutic effect desired in the treatment of acute leukemia of childhood. However, because of extreme potency and narrow margin of safety, therapy with the folic acid antagonists can be hazardous; hematopoietic response is sometimes very difficult to control, and even small errors in dosage can lead to irreversible bone marrow depression. In such situations, leucovorin calcium exerts a potent antidotal action since it provides an exogenous source of the active hematopoietic principle, the biosynthesis of which is blocked. There is adequate laboratory and clinical evidence to show that prompt administration of the drug after overdosage with any of the folic acid antagonists results in a reversal of both hematopoietic toxicity and the generalized toxic effect on all reticuloendothelial tissue. Whenever possible, therapy with leucovorin calcium should be initiated before susceptible cell groups have become too damaged by folic acid antagonists to be responsive to antidotal action. Hence, in cases of inadvertent overdosage, leucovorin should be administered as soon as the error is detected; if a period of more than four hours intervenes, the drug may not be effective. Leucovorin calcium should not be administered simultaneously with folic acid antagonists in an attempt to modify or abort clinical toxicity. Such a regimen may nullify completely the desired therapeutic effect. If signs of toxicity appear after use of the folic acid antagonists, the offending drug should be withdrawn immediately, and, along with general supportive measures, leucovorin calcium should be administered on a daily basis until hematological and clinical improvement is noted.

Because leucovorin calcium supplies the active metabolite needed for the proliferation and maturation of blood cellular elements, it is effective in ameliorating the blood picture in the megaloblastic anemias associated with pregnancy, infancy, sprue, and nutritional deficiency. However, the ability of the blood-forming organs to convert folic acid to the citrovorum factor is not impaired in these anemias. Accordingly, in the megaloblastic anemias, no particular purpose is accomplished by using leucovorin calcium, which must be injected parenterally, instead of folic acid, which may be taken orally.

Before the introduction of cyanocobalamin (vitamin B_{12}), leucovorin calcium was used for the treatment of pernicious anemia. The action of the drug in this condition is essentially the same as that of folic acid. Thus, while leucovorin calcium may restore to normal the blood picture in patients with pernicious anemia, it is ineffective in the control of neurological symptoms. Cyanocobalamin, which overcomes both the hematological and neurological effects of pernicious anemia, has displaced both folic acid and leucovorin calcium in the treatment of this condition.

In therapeutic doses, leucovorin calcium appears to be essentially nontoxic. To date, no untoward effects or adverse reactions referable to the drug have been reported.

Dosage

Leucovorin calcium is administered intramuscularly. To counteract the toxic effects of folic acid antagonists, the usual dose is 3 to 6 mg. per day. This is continued as long as signs of toxicity persist. For the treatment of megaloblastic anemias, a dose of 10 mg. may be injected daily for 10 to 15 days. Subsequent therapy and dosage is dependent upon the hematological response as reflected by both peripheral blood cell counts and bone marrow aspirations. Dosage of leucovorin calcium as an adjunct to cyanocobalamin therapy in the treatment of pernicious anemia has not been well defined, but amounts ranging from 0.2 to 15 mg. per day have been employed in this condition.

Applicable commercial name: Leucovorin.
Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of leucovorin calcium.
***J. Am. Med. Assoc.* 164:2047 (Aug. 31) 1957.**

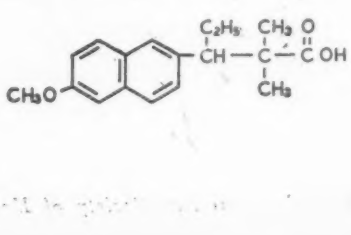
Preparations

Injection Leucovorin Calcium 3 mg. per ml.; 1 ml. ampuls.

Methallenestril

Vallestril®

METHALLENESTRIL is α,α-dimethyl-β-ethyl-6-methoxy-2-naphthalenepropionic acid.—3-(6-Methoxy-2-naphthyl)-2,2-dimethylpentanoic acid.—The structural formula of methallenestril may be represented as follows:



Actions and Uses

Methallenestril, a nonsteroid estrogenic compound, is effective orally, and its onset of action is prompt. Its estrogenic potency, milligram for milligram, is apparently no greater than that of orally administered estrone; it is only about one-tenth as potent as diethylstilbestrol. Methallenestril causes less gastrointestinal upsets than does diethylstilbestrol. Otherwise, its administration in therapeutically effective doses is followed by about the same degree of nausea as is found with the other synthetic estrogens. In the reports available to date, there is some indication that methallenestril therapy may cause less withdrawal bleeding than do the other estrogens. However, if dosage is adjusted sufficiently to produce a comparable therapeutic effect, endometrial proliferation and subsequent withdrawal bleeding may be expected. Methallenestril is useful for the same conditions for which other natural and synthetic estrogens are employed and is subject to the same contraindications. (See the general statement on estrogens in New and Nonofficial Remedies.)

Dosage

Methallenestril is administered orally. The usual initial dosage for menopausal symptoms is 6 mg. daily for three weeks; thereafter dosage is decreased to 3 mg. daily for as long as required. For suppression of lactation, 20 mg. is administered daily for the first five postpartum days. Doses of 6 mg. daily for four weeks may be given for the treatment of postmenopausal vaginitis, kraurosis vulvae, and pruritus vulvae. In the initial treatment of postmenopausal osteoporosis, 9 mg. per day for two weeks is usual; maintenance dosage is 3 mg. daily. For the palliation of prostatic carcinoma, daily doses of 20 mg. may be administered.

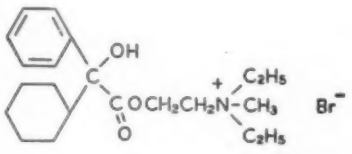
Preparations: tablets 3 mg. and 20 mg.
Applicable commercial name: Vallestril.
G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of methallenestril.
***J. Am. Med. Assoc. 165*:156 (Sept. 14) 1957.**

Preparations

Tablets Methallenestril (Vallestril) 3 mg. and 20 mg.

Oxyphenonium Bromide — Antrenyl® Bromide

OXYPHENONIUM BROMIDE is diethyl(2-hydroxyethyl) methylammonium bromide α-phenyl-α-cyclohexylglycolate.—The structural formula of oxyphenonium bromide may be represented as follows:



Actions and Uses

Oxyphenonium bromide, a synthetic quaternary ammonium compound, is used clinically as an anticholinergic agent. Its pharmacological actions, side-effects, and chemical structure are similar to those of tricyclamol chloride, tridihexethyl iodide, and hexocyclium methylsulfate. In addition to producing an antispasmodic effect on the musculature of the gastrointestinal tract, oxyphenonium bromide also diminishes gastric secretion. Thus, it is useful for the adjunctive management of peptic ulcer and for other disorders of the gastrointestinal tract, characterized by hypermotility or spasm, that are usually amenable to anticholinergic therapy. It may also be used in place of atropine or scopolamine as a pre-anesthetic medication in patients who are sensitive to the belladonna alkaloids. Currently available evidence confirms the usefulness of oxyphenonium bromide as a potent antispasmodic but does not indicate any advantages that would distinguish the drug from other agents in this category.

Side-effects of oxyphenonium bromide include those of the anticholinergic agents in general. Blurring of vision, dryness of the mouth, difficulty in urination, and constipation may follow its clinical use. Less common reactions have included weakness, dizziness, drowsiness, nausea, vomiting, headache, and tachycardia. The drug is contraindicated in the presence of glaucoma, prostatic hypertrophy, and pyloric obstruction.

Dosage

Oxyphenonium bromide is given orally, subcutaneously, or intramuscularly. When immediate action is desired in severe gastrointestinal spasm with pain, 1 to 2 mg. (0.5 to 1 cc. of a 0.2% solution) may be injected subcutaneously or intramuscularly every six hours; oral therapy should then be substituted as soon as possible. The usual oral dosage for adults is 10 mg. four times daily. Dosage should be adjusted, however, according to individual response and the appearance of side-effects. For children, dosage is reduced proportionally according to age.

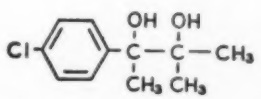
Applicable commercial name: Antrenyl Bromide.
Ciba Pharmaceutical Products Inc. cooperated by furnishing scientific data to aid in the evaluation of oxyphenonium bromide.
***J. Am. Med. Assoc. 164*:2047 (Aug. 31) 1957.**

Preparations

Injection Oxyphenonium (Antrenyl)) Bromide 2 mg. per ml.; 10 ml. vials.
Solution, Pediatric, Oxyphenonium (Antrenyl) Bromide 1 mg. per drop; 5 ml. bottles.
Syrup Oxyphenonium (Antrenyl) Bromide 5 mg. per 4 ml.; pint bottles.
Tablets Oxyphenonium (Antrenyl) Bromide 5 mg.
Tablets Oxyphenonium (Antrenyl) Bromide 5 mg. with Phenobarbital 15 mg.

Phenaglycodol — Ultran®

PHENAGLYCODOL is 2-*p*-chlorophenyl-3-methyl-2,3, butanediol.—The structural formula of phenaglycodol may be represented as follows:



Actions and Uses

Phenaglycodol is one of a series of synthetic diol compounds that exert a mild depressant effect on the central nervous system. At least at the level of the spinal cord, the drug has properties in common with the interneuronal blocking agents such as mephenesin and meprobamate. Phenaglycodol and meprobamate have a common chemical derivation from mephenesin. In the case of phenaglycodol, a degree of metabolic stabilization is achieved by full substitution on the OH-bearing carbon atoms. In experimental animals, phenaglycodol

produces some degree of skeletal muscle relaxation and exerts an inhibitory influence on transmission through polysynaptic pathways. It also diminishes the severity of electrically induced convulsions in animals, and initial clinical experience has suggested a possible usefulness in epilepsy. As a muscle relaxant, phenaglycodol is much less potent that mephenesin. From the standpoint of overall clinical usefulness, phenaglycodol is probably most closely comparable to meprobamate. Hence, it may be characterized as a mild sedative with weak muscle-relaxing properties.

Phenaglycodol has been used to produce a calming or mood-ameliorating effect in patients with emotional instability, anxiety-tension states, and functional disorders. Although early reports have been favorable, there is need for more evidence to establish conclusively its usefulness as a psychotherapeutic agent. Studies designed to compare its tension-relieving effects with meprobamate are inconclusive. In some patients with anxiety states, the drug has elicited a degree of behavioral improvement; in other studies the effect has been primarily that of a placebo. In general, phenaglycodol appears to be similar in effectiveness to meprobamate, but the ultimate usefulness of this type of drug must await the results of further clinical experience.

From the evidence available to date, it would appear that phenaglycodol may have usefulness in the adjunctive management of simple neuroses. The drug probably has no place in the treatment of the more severe psychotic type of mental disturbance and cannot be classified as a tranquilizing agent in the same sense as chlorpromazine or reserpine.

The toxicity of phenaglycodol is low. No adverse effects on hepatic or hematopoietic function have been observed after long-term administration to animals and patients. In clinical experience, large doses are apparently without effect on blood pressure, pulse, or respiration. To date, drowsiness appears to be the only side-effect referable to therapy with phenaglycodol. This has occurred only occasionally and generally follows the administration of high doses.

Dosage

Phenaglycodol is administered orally. The usual dosage for adults is 300 mg. three or four times daily.

Preparations: tablets 300 mg.
Applicable commercial name: Ultran.
Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of phenaglycodol.
J. Am. Med. Assoc. ***165:157*** **(Sept. 14) 1957.**

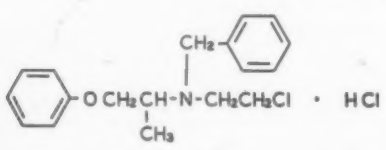
Preparations

Capsules Phenaglycodol (Ultran) 0.3 Gm.

Phenoxybenzamine Hydrochloride

Dibenzyline® Hydrochloride

PHENOXYBENZAMINE HYDROCHLORIDE is N-(2-chloroethyl)-N-(1-methyl-2-phenoxyethyl)benzylamine hydrochloride.—The structural formula of phenoxybenzamine hydrochloride may be represented as follows:



Actions and Uses

Phenoxybenzamine hydrochloride is a potent adrenergic blocking agent of the β-haloalkylamine series. The pharmacology of this drug and that of its closely related congener, dibenzyl-β-chlorethylamine (Dibenamine), have been carefully studied. The drug selectively blocks the excitatory response of smooth muscle and exocrine glands to epinephrine but does not abolish the inhibitory response of smooth muscle or the myocardium to epinephrine-like agents. Thus, adrenergic blockade with phenoxybenzamine has been compared to "chemical sympathectomy." As with all agents in this category, phenoxybenzamine blocks the response to endogenous or exogenous epinephrine more effectively than it blocks the response to adrenergic nerve stimulation. Hence, the separation of adrenergic blocking agents into adrenolytic and sympatholytic drugs is now believed to be largely artificial, although phenoxybenzamine would ordinarily be considered a representative of the former. The drug reduces or abolishes the pressor response not only to epinephrine but to other sympathomimetic amines as well; in experimental animals, adrenergic blockade with phenoxybenzamine protects against doses of epinephrine that would ordinarily be supralethal. Before adrenergic blockade has been completed, the effects of the drug can be overcome by large doses of epinephrine. Once full blockade has been produced, however, neither epinephrine or any other drug now known will break through it, and this blocking action is persistent. The precise site of adrenergic blockade with phenoxybenzamine has been accurately pinpointed. Studies have shown conclusively that the drug does not alter or block the release of adrenergic mediator, influence thoracolumbar (sympathetic) outflow or spinal reflex arcs, cause sympathetic ganglionic blockade, nor alter the ability of smooth muscle to contract to nonsympathomimetic musculotropic stimuli. Hence, the drug acts directly and specifically on adrenergic receptor cells in a noncompetitive manner in such a way that the receptiveness to adrenergic (sympathomimetic) stimuli is decreased or abolished.

Although phenoxybenzamine hydrochloride is sparingly soluble in water, at least 20 to 30% of an orally administered dose is absorbed in an active form from the gastrointestinal tract. The duration of action of the drug is prolonged; after a single full dose, adrenergic blockade persists for three to four days or longer. Approximately 50% of the drug appears in the urine and bile within 12 hours after oral administration.

Except for a mild antihistaminic action and moderate miosis, the effects of the drug are predominately those of peripheral vasodilation. Thus, increases in peripheral blood flow and skin temperature and a lowering of blood pressure in patients in both supine and erect positions are the outstanding effects of adrenergic blockade with this agent. The drug also suppresses the hyperglycemic response to epinephrine and blocks epinephrine-induced discharge of corticotropin. The ancillary actions of phenoxybenzamine are minimal; it has no effect on the parasympathetic system and produces only negligible changes in gastrointestinal tone and motility.

Phenoxybenzamine and related β-haloalkylamines previously were considered interesting and valuable laboratory tools for pharmacological research but of little clinical usefulness. However, with the elucidation of the discrete adrenergic blocking properties of these compounds, it became apparent that they might prove useful for the treatment of certain peripheral vascular

IN INTRAVENOUS ANESTHESIA

Neraval
SODIUM

"... the shortest-acting thiobarbiturate so far known to us ..."[1]

- **Shorter duration of effect**[1]
- **More rapid, complete recovery**[3,5-7]
- **Diminished cumulative action**[2-4,6,8]

HOW YOUR PATIENT BENEFITS

- Rapid, pleasant recovery.
- Unusual freedom from prolonged postanesthetic depression or "hangover."
- Shortened period of postoperative incapacity.
- Heightened patient morale.

HOW YOUR HOSPITAL BENEFITS

- Less-crowded recovery rooms.
- Shortened postoperative recovery period permits earlier assignment of nurses to other hospital duties.[1]

PACKAGING

NERAVAL Sodium Sterile Powder: vials of 1 Gm. and 2 Gm., boxes of 6 and 25; vials of 5 Gm., boxes of 1 and 25.

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(1) Boone, J.D.; Munoz, R., and Dillon, J.B.: Anesthesiology *17*:284, 1956. (2) Zima, O.; von Werder, F., and Hotovy, R.: Anaesthesist *3*:244, 1954. (3) Fitzpatrick, L.J.; Clarie, D'A., and Mersch, M.A.: To be published. (4) Blake, M.W., and Perlman, P:L.: J. Pharmacol. & Exper. Therap. *117*:287, 1956. (5) Ayd, F.J., Jr.: Neraval: A new anesthetic for electroconvulsive therapy, Paper presented at annual meeting, Electroshock Research Association, Chicago, Illinois, April 29th, 1956. (6) Irwin, S.; Stagg, R.D.; Dunbar, E., and Govier, W.M.: J. Pharmacol. & Exper. Therap. *116*:317, 1956. (7) Reifferscheid, M., and Dietmann, K.: Deutsche med. Wchnschr. *79*:638, 1954. (8) Dietmann, K.: Deutsche med. Wchnschr. *79*:1748, 1954.

NERAVAL® Sodium, brand of methitural sodium.

Schering

NE-J-5116

diseases. Subsequent clinical trials have confirmed not only their efficacy for this purpose but also the superiority of phenoxybenzamine hydrochloride over other chemically related compounds in the series. As might be expected from its pharmacological actions, phenoxybenzamine is more effective in those peripheral vascular diseases characterized by excessive vasospasm than in those of the organic occlusive forms. Thus, the drug is of value in such conditions as Raynaud's syndrome, acrocyanosis, causalgia, chronic vasospastic ulceration of extremities, and frostbite sequelae; it may also be of value in those forms of obliterative or obstructive arterial disease that are complicated by vasospasm of vessels remaining patent. Because of its specificity, effectiveness when given orally, and prolonged action, it is considered preferable to other available adrenergic blocking agents for the medical management of these conditions. If sufficient time is allowed for full adrenergic blockade to develop, a large percentage of patients with vasospastic involvement may be expected to show objective and subjective improvement, including relief of causalgic pain, healing of lesions, clearing of cyanosis or ischemia, and increase in skin temperature. The drug is considered by some authorities to be superior to cervical sympathectomy for most cases of bilateral digital ischemia of the upper extremities, and its therapeutic trial is indicated in cases of severe causalgia before sympathectomy is performed. In patients hospitalized for acute peripheral vascular accidents, phenoxybenzamine also appears to be useful to combat reflex spasm of collateral vessels and of the originally occluded vessel after embolectomy. It has been administered to patients with such conditions as thromboangiitis obliterans (Buerger's disease) and intermittent claudication, but the results have been only fair.

Phenoxybenzamine hydrochloride has been employed for the management of moderate to severe hypertension. Although high doses undoubtedly lower blood pressure, clinical experience has indicated that excessive postural hypotension and other undesirable effects usually outweigh the benefits attained. Hence, the drug is no longer considered useful for this purpose when employed alone. It has, however, been combined in small amounts with the alkaloids of Rauwolfia and Veratrum for the management of hypertension. Other experimental uses of the drug have included the treatment of toxemia of pregnancy, cardiospasm, glaucoma, and the preoperative management of pheochromocytoma. At present there is insufficient evidence to justify the use of the drug in any of these conditions. Since phenoxybenzamine blocks the excitatory but not the inhibitory response of smooth muscle to epinephrine, it has been employed intravenously in patients with status asthmaticus to permit the safer administration of exceedingly large doses of epinephrine. While this is a logical clinical application of the drug's pharmacological actions, this use should at present be considered experimental.

Most of the side-effects of phenoxybenzamine result from the ability of the drug to produce adrenergic blockade and may be considered for the most part extensions of the therapeutic action. The side-effects most commonly encountered are nasal congestion, miosis, tachycardia, and postural hypotension. Occasionally, sedation and drowsiness occur, and male patients sometimes experience failure of ejaculation. Since the drug blocks salivation in those glands innervated by sympathetic fibers, some degree of xerostomia may occur. The drug produces little, if any, gastric distress, nausea, or vomiting. Most side-effects tend to decrease as therapy is continued. The development of some tolerance after prolonged therapy is likely, although complete refractoriness to the drug is rare.

Phenoxybenzamine is contraindicated in any condition in which a fall in blood pressure may be undesirable or dangerous. It should be given with extreme caution to hypertensive patients with cerebral atherosclerosis or renal damage. In patients with compensated congestive heart failure or coronary artery disease, the tachycardia that sometimes accompanies high doses may precipitate frank failure and anginal attacks. Adverse hematopoietic effects from phenoxybenzamine have not been reported in either laboratory studies or clinical use.

Dosage

Phenoxybenzamine hydrochloride is administered orally. Dosage is variable and must be individualized according to the therapeutic response and the appearance of side-effects. As a general guide, 10 to 20 mg. once daily may be given to initiate therapy. After four days at this dosage, the daily amount is increased by 10 mg. and thereafter increased by similar increments until a satisfactory response is obtained. The usual maintenance dosage ranges from 20 to 60 mg. once or twice daily. In some patients, particularly those in whom hypertension is present, dosages of 0.2 Gm. or more per day may be necessary. At least two weeks or more are required before full adrenergic blockade develops and maximal therapeutic results are obtained.

Applicable commercial name: Dibenzyline.

Smith, Kline & French Laboratories cooperated by furnishing scientific data to aid in the evaluation of phenoxybenzamine hydrochloride.

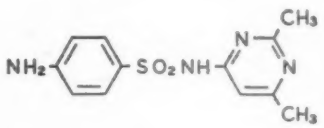
J. Am. Med. Assoc. *164*:1756 (Aug. 17) 1957.

Preparations

Capsules Phenoxybenzamine (Dibenzyline) Hydrochloride 10 mg.

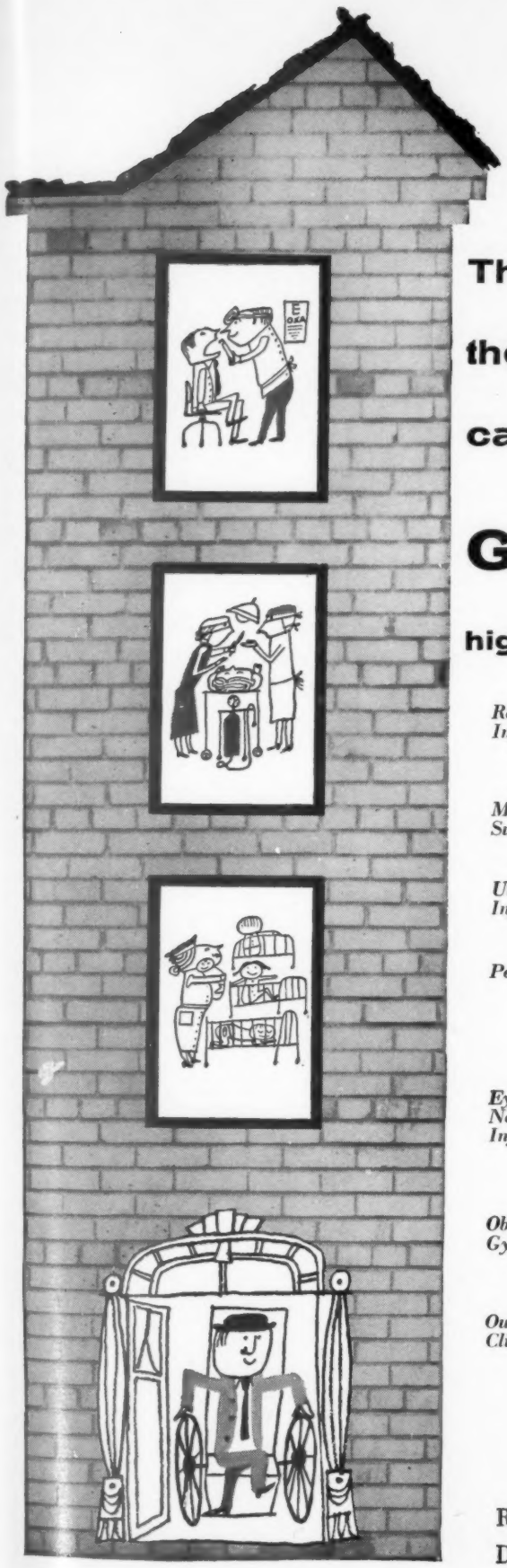
Sulfisomidine — Elkosin®

SULFISOMIDINE is N'-(2,6-dimethyl-4-pyrimidinyl)sulfanilamide.—The structural formula of sulfisomidine may be represented as follows:



Actions and Uses

Sulfisomidine, a structural isomer of sulfamethazine, is useful for the treatment of systemic and urinary tract infections caused by microorganisms that are susceptible to the bacteriostatic effects of sulfonamides. In contrast to most other agents in this class, sulfisomidine is not readily acetylated in the body. Thus, after oral administration, only about 5 to 10% of total blood sulfonamide is conjugated, and about 90% of the drug appears in the urine in the free form. Since the free form of the drug is soluble in acid urine, sulfisomidine compares favorably with the other sulfonamides with respect to renal toxicity. Hematuria and crystalluria are only rarely encountered. Hence, concomitant alkalinization of the urine is not necessary to increase the solubility of the drug. As with all sulfonamide therapy, however, fluid intake should be maintained above 1.5 liters daily.



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highly soluble, single sulfonamide

Respiratory Infections	tablets, 0.5 Gm each
Meningitis Surgery	ampuls, 5 cc (2 Gm) and 10 cc (4 Gm)
Urinary Infections	tablets, 0.5 Gm each
Pediatrics	pediatric suspension (raspberry-flavored), and syrup (chocolate-flavored), containing the new, tasteless Gantrisin (acetyl)
Eye, Ear, Nose & Throat Infections	ophthalmic solution, 4%, ophthalmic ointment, 4%, ear solution, 4%, and nasal solution, 4%
Obstetrics & Gynecology	vaginal cream, 10%, in white vanishing cream base
Outpatient Clinic	tablets, 0.5 Gm each

Gantrisin®—brand of sulfisoxazole
Gantrisin® (acetyl)—brand of acetyl sulfisoxazole

Roche Laboratories
Division of Hoffmann-La Roche Inc • Nutley • N. J.

635

Aside from diminished renal toxicity, the side-effects of sulfisomidine are similar to those of other sulfonamides. (See the general statement on sulfonamides and on pyrimidine derivatives in New and Nonofficial Remedies.)

Dosage

Sulfisomidine is administered orally. The initial dose in severe infections is calculated on the basis of 0.1 Gm. per kilogram of body weight. Subsequent doses of one-sixth the initial dose should be given every four hours (six times a day) until the infection is well under control. Then dosage is decreased to four times a day until a cure is effected.

Applicable commercial name: Elkosin.
Ciba Pharmaceutical Products Inc. cooperated by furnishing scientific data to aid in the evaluation of sulfisomidine.

J. Am. Med. Assoc. 164:2048 (Aug. 31) 1957.

Preparations

Syrup Sulfisomidine (Elkosin) 0.25 Gm. per 4 ml.; pint bottles.
Tablets Sulfisomidine (Elkosin) 0.5 Gm.

Report to the Council

The following report, prepared by the Council on Drugs at the request of the Special Committee on Influenza, is presented as a matter of scientific information for the medical profession.

HAROLD C. LUETH, *Chairman.*

Antibiotics and Influenza

The explosive outbreak of influenza during the past spring in the Orient, together with is erratic spread to Europe and the Western hemisphere, has recalled to the minds of many physicians the pandemic of influenza of 1918-1919. In the spring of 1918, a mild but widespread and explosive epidemic of influenza broke out in Europe. In many military units on the Western Front, the incidence of influenza reached a rate of 50% within a period of 10 days to 2 weeks. Certain civilian communities in Europe had comparable incidences of this mild type of influenza. The disease, in the spring of 1918, had a very low mortality rate and practically disappeared from the fighting forces and civilian communities by July 1, 1918. However, in September and in succeeding months influenza returned, and all communities in the world except those that were completely isolated (Tristan da Cunha, for example) were stricken by the infection. In its waves in 1918 and 1919, the disease was characterized by (1) a high morbidity rate, (2) an ability to injure the lungs, thus facilitating the invasion of micro-organisms which produced pneumonia, and (3) a high case fatality rate among those patients who developed pneumonia. It has been estimated that 20 to 30 million people died during this pandemic.

The influenza viral infection in the fall and winter of 1918-1919, while prostrating in effect, did not kill in itself except rarely. Pneumonia and it complications produced by beta-hemolytic streptococci, micrococci (staphylococci), pneumococci, influenza bacilli, and rarely by certain other organisms were responsible for the deaths.

There has been a close and disturbing parallel between the outbreaks of influenza which have been observed in Asia during the past spring and which spread to the Western world and the vernal appearance of what was called Spanish influenza in 1918. The question which is agitating the minds of many physicians at the moment is whether they will witness this fall a recrudescence of influenza throughout the world comparable in incidence and severity (as far as secondary infection is concerned) with that which occurred in the winter of 1918-1919.

Should this occur, what policies should guide the physician relative to the prophylaxis and treatment of secondary bacterial infection in patients suffering from influenza? After a careful consideration of this whole problem, the Council on Drugs makes the following suggestions:

1. Since sulfonamides and antibiotics have no therapeutic effect on the viruses of influenza, their use in the primary treatment of influenza would be contrary to good medical practice.

2. Antibacterial compounds such as sulfonamides or antibiotics should not be generally used in the prophylaxis of bacterial infection in patients ill with influenza. The prime reason for this recommendation is to prevent the development of disease-producing strains of micro-organisms which would be resistant to sulfonamide or antibiotic therapy. The secondary reason is to obviate the development of reactions of sensitivity or of direct toxicity to antibiotics or sulfonamides. The possible exceptions to this injunction are (*a*) pregnant women, debilitated infants, and older individuals, (*b*) patients being treated for other bacterial infections with sulfonamides or antibiotics who develop influenza, and (*c*) patients suffering from chronic, nonallergic respiratory tract disease.

3. All patients ill with influenza in whom it has been demonstrated that secondary bacterial infections have developed should be treated with a sulfonamide or antibiotic of choice. In general, the following recommendations can be made as to the choice of sulfonamides and antibiotics: (*a*) pneumococcic pneumonia: penicillin, broad-spectrum antibiotic, sulfonamide; (*b*) beta-hemolytic streptococcic pneumonia: penicillin, broad-spectrum antibiotic, sulfonamide; (*c*) influenzal bacillary pneumonia: broad-spectrum antibiotic; (*d*) micrococcic pneumonia: this will be a real problem because of the resistance of strains of these organisms to sulfonamides and antibiotics. Careful testing of the sensitivity to the various antibiotics of micrococci isolated from patients ill with pneumonia should be done and the choice of the antibiotic made upon data garnered from these tests. If the condition of the patient is so grave as to necessitate immediate therapy, massive intravenous doses of penicillin plus 1 Gm. of streptomycin per day may be administered while the results of antibiotic sensitivity tests are being awaited.

Finally, a word of caution should be raised relative to the hospitalization of patients ill with influenza. It is the carefully considered opinion of the Council on Drugs that patients ill with uncomplicated influenza should be treated at home. It is a well-demonstrated fact that in many hospitals a high percentage of personnel such as doctors, nurses, and attendants may be carriers of micrococci which are resistant to antibiotic or sulfonamide therapy. A patient ill with primary influenza who is introduced into such an environment would certainly be in jeopardy of contracting a micrococcic pneumonia which could not be cured by antibiotic or sulfonamide therapy.

J. Am. Med. Assoc. 165:58 (Sept. 7) 1957

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Report to the Council

Asian Influenza — Current Status of

The following report has been compiled from late data furnished to the American Medical Association's Special Committee on Influenza by the Communicable Disease Center of the Public Health Service, U. S. Department of Health, Education, and Welfare. Progress reports on Asian influenza will be transmitted to the profession regularly as long as there is a possibility of an epidemic.

HAROLD C. LUETH, *Chairman.*

There appears to be an increase of influenza-like illness in further civilian groups. A school-centered outbreak has occurred in Mississippi and a housing development has been affected in California. A Florida community also appears to have experienced an increased incidence of influenza-like illness in the past week.

Outbreaks and cases of influenza due to Asian strains were confirmed during the period June 1-Aug. 22 in the following locations: California (San Francisco, San Diego, Monterey, Davis, San Mateo, Los Angeles), Virginia (Norfolk), Rhode Island (Newport), Hawaii, Ohio (Cleveland), Iowa (Grinnell), Utah (Salt Lake City), Kansas, (Topeka), Maryland, Kentucky (Louisville, Morris Fork), Pennsylvania (Valley Forge, Lancaster, Old Forge), Texas (Corpus Christi, Bexar County), Washington (Seattle), Nebraska (Omaha), Florida (Jacksonville, Miami, St. Petersburg), Michigan (Calhoun County, Bay County, Coldwater), Louisiana (Grant Parish, Tangipahoa Parish, New Orleans), New Jersey (Burlington County), New York (Cayuga County, New York City), Oregon.

Reactions to Influenza Vaccine Containing Asian Strain Virus

Of 239 volunteers vaccinated with monovalent Asian strain influenza vaccine, 158 were examined and questioned, for the purposes of this report, concerning postvaccination reactions. Injections were given intramuscularly over the deltoid area, and subjects were approached two or three days later. Vaccination groups included one each at 50, 100, and 200 CCA (chick cell agglutination) units and an equal number of saline and aluminum phosphate adjuvant subjects at each dosage level.

The volunteers were examined or questioned for evidence of local erythema and pain or swelling and any other postvaccination symptoms. *Any* affirmative reply was considered a positive reaction regardless of whether mild or severe. Care was taken to differentiate immediate injection pain and venipuncture discomfort from postvaccination signs and symptoms.

Reaction to Monovalent Asian Strain Influenza Vaccine

Reaction	% of 48 People Questioned After Dose of 50 CCA Units	% of 53 People Questioned After Dose of 100 CCA Units	% of 57 People Questioned After Dose of 200 CCA Units
Fever	6	8	14
Generalized pain in extremity*	21	23	54
Local swelling*	2	11	18
Local pain at injection site*	17	19	42

* Includes mild through severe reactions.

With the one exception noted below no severe reactions occurred. Symptoms were primarily those noted in the table and, with rare exceptions, lasted no longer than 12 to 24 hours. An increase in reactions was seen as the dosage of vaccine increased. Among those who had febrile reactions, only three were concerned enough to actually record their temperatures. Other symptoms mentioned in a few instances included malaise, myalgia, and headache. These were unrelated to dosage of vaccine. Differences in reaction to saline and adjuvant vaccines were not significant.

A single subject experienced sufficient fever, malaise, and myalgia to lose one-half day of working time. Otherwise, the symptoms noted were so mild that normal clerical activities were not interfered with or the subjects made unduly uncomfortable.

J. Am. Med. Assoc. 165:59 (Sept. 7) 1957.

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary*

Treatment of Gout — Current Status

WILLIAM D. ROBINSON, M.D., ANN ARBOR, MICH.

Substantial advances in the management of gout have been made in recent years. Acute attacks of gout can now be terminated rapidly in most patients by the use of one of several medicaments. By proper management, the frequency of such attacks can be diminished and the later complications of the disease minimized or prevented. Although there is no known cure for gout in the strict sense of the word, results with the measures now available, if adapted to the stage of the disease and the needs of the individual patient, are distinctly better than those that could be obtained previously.

Diagnosis

Although gout is less common than some other forms of joint disease, it is by no means rare. It constitutes approximately 5% of the diagnoses in patients attending clinics devoted to arthritis and related diseases. The most important factor in establishing the correct diagnosis is to keep the possibility of gout in mind. The overwhelming preponderance of the disease in males and the characteristics of the acute attack, with an acute inflammatory reaction in or around one or a few joints developing in a relatively short time and subsiding after a few days or weeks without residual impairment of joint function, are well recognized. The only pathognomonic finding is the demonstration of urate crystals in the soft tissues, as in the tophi of the ears; however, this finding actually represents a late complication of gout in a situation that should have been diagnosed many years before. The roentgenographic appearance of punched-out lesions in the bones near the joint surface is suggestive of gout but cannot be considered pathognomonic. Exactly the same type of lesion may be seen in other forms of joint disease, and, since these lesions represent osseous tophi, they are a late manifestation of the disease.

An accurate diagnosis of pretophaceous gout can be made on the combination of three finds: the characteristics of the acute attack, the demonstration of an elevated serum urate level, and the therapeutic response to an intensive course of colchicine, properly administered. Many drugs taken for relief of acute articular pain usually cause a temporary decrease in

From the Department of Internal Medicine and the Rackham Arthritis Research Unit, University of Michigan.

the serum urate level that may interfere with diagnostic studies. Such decreases may follow administration of salicylates, phenylbutazone (Butazolidin), probenecid (Benemid), corticotropin (Acth, Acthar, Corticotropin, Depo-Acth) and cortisone (Cortisone, Cortogen, Cortone) or related adrenocortical steroids. Colchicine does not alter the serum urate level.

Primary or idiopathic gout is associated with a genetically controlled abnormality of body chemistry, which is characterized by an elevation in the level of urates in the blood. Studies with isotopic tracer techniques indicate that these patients have an increase in the "miscible pool" of urates in the body and that in at least a portion of these patients the hyperuricemia is attributable to overproduction of urates. However, the exact relationship between the hyperuricemia and the acute attack of gout remains obscure. There is no consistent alteration in the concentration of the urate in the blood at the time of acute attacks, nor is there evidence to indicate any acceleration of deposition of uric acid immediately before or during acute articular symptoms. On the other hand, the late complications of gout center around the deposition of urates in cartilage, soft tissue, and kidneys; such deposition is undoubtedly influenced by the duration and degree of hyperuricemia. These facts have definite implications with respect to the therapy of gout. Measures effective in the treatment or prevention of acute attacks often have no effect on the hyperuricemia. Measures directed at lowering the abnormally elevated blood uric acid level are ineffective in the treatment of the acute attack but are of vital importance in the prevention or correction of the late complications of gout.

Treatment of Acute Attacks of Gout

Therapeutic measures are determined by the stage of the disease in the patient. At least three drugs are reliable and effective in the relief of acute gout.

Colchicine is a specific for gout and, if properly used, remains the most useful drug in the treatment of this disorder. Colchicine is available in tablet sizes of 0.5 or 0.65 mg. At the onset of symptoms, 0.5 (or 0.65) mg. should be administered orally every hour, or 1 mg. may be given every two hours. This dosage is continued without interruption until one of three things happens: pain is relieved; nausea or diarrhea develops; or a total of 7.5 to 10 mg. (according to the patient's weight) has been taken. When treatment is begun at the very onset of acute symptoms, the attacks can usually be terminated before gastrointestinal symptoms develop. In an established attack, however, relief usually will not be obtained until the patient experiences some nausea or diarrhea. To avoid unpleasant purgation, it is important to emphasize to the patient that the first loose stool constitutes diarrhea and that even if pain has not been relieved at this point, no further colchicine should be taken. A prescription for camphorated opium tincture(paregoric) should be written at the time that the colchicine is prescribed, with instructions that 4 cc. should be taken after each loose stool or every three hours for nausea.

The tolerated dosage of colchicine is relatively constant for each patient. Therefore, the patient should be instructed to note the number of doses taken in the treatment of his first attack. In subsequent attacks, administration of colchicine can be stopped one or two doses short of the amount that produces diarrhea. When a course of colchicine fails to relieve symptoms completely, or when symptoms have been relieved and then recur, the course may be repeated after a lapse of at least 48 hours. After a course of colchicine has been completed, maintenance treatment with the drug in dosages of 1 to 1.5 mg. a day should be instituted and continued for at least three weeks.

Colchicine is also effective when given intravenously, the usual total effective dosage ranging from 1 to 3 mg. The initial dose may be 1 or 1.5 mg., with subsequent doses of 0.5 to 1 mg. given every six hours until pain is relieved. Gastrointestinal symptoms may occur if the total dose exceeds 3 mg. Care must be taken to insure that the injection is made intravenously, as colchicine solution is irritating if injected outside the veins.

Since colchicine has no significant effect on other types of acute inflammation, including other forms of acute arthritis, the response to intensive use of this agent may be helpful in confirming the diagnosis. The initial effect is essentially a subjective one, with relief of the excruciating aspects of the pain and of the patient's apprehension that pain may be produced by jarring or movement. An additional 12 to 24 hours may elapse before there is convincing decrease in the objective evidences of inflammation, and three to four days may elapse before edema and tenderness have subsided.

Phenylbutazone is also effective in the treatment of acute gouty attacks. Effective control is usually obtained within 24 to 48 hours with a dosage of about 0.8 Gm. daily. Treatment may be initiated with a dose of 0.4 Gm. and subsequent doses of 0.2 Gm. given at intervals of four to six hours until pain has been relieved. Phenylbutazone is not recommended for maintenance therapy; therefore, the patient should be treated with maintenance dosage of colchicine after the acute attack has been controlled. Phenylbutazone has toxic potentialities including gastrointestinal irritation, hematemesis, granulocytopenia, sodium and water retention with edema, and, not infrequently, hypersensitivity skin reactions. Although these reactions are less likely to occur when the drug is used only for a few days, nevertheless, vigilance in observing patients receiving this drug is essential.

Administration of corticotropin in combination with a maintenance oral dosage of colchicine is also satisfactory in relieving acute gout within a few hours. Long-acting preparations, usually purified corticotropin in a gelatin vehicle, are most convenient when administered as a single intramuscular injection equivalent to 100 U. S. P. units of corticotropin; only occasionally is a second injection required 24 hours later. Aqueous solutions of corticotropin may be administered intramuscularly in doses of 50 U. S. P. units every six hours until relief is obtained; or corticotropin may be administered as a slow intravenous drip over a period of eight hours, in doses of 20 U. S. P. units in 500 cc. of a 5% dextrose solution. Colchicine is given orally in doses of 0.5 mg. every six hours after an initial injection of corticotropin and its administration continued until diarrhea occurs, usually within three to five days; the amount of colchicine given is then adjusted to maintenance levels.

In our experience, the use of adrenocortical steriods (glucocorticoids), cortisone and hydrocortisone (Cortef, Cortril, Hydrocortone), and their synthetic analogs, prednisone (Deltasone, Deltra, Meticorten) and prednisolone (Delta Cortef, Hydeltra, Meticortelone), has not given as reliable or as consistent results in the treatment of acute gouty attacks as the use of colchicine, phenylbutazone, or corticotropin. However, these preparations are at times useful in patients who do not respond well to colchicine or phenylbutazone and in

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1. Colavincenzo, J. W., and others: Pennsylvania M. J. 59:338 (March) 1956.
2. Ansbro, F. P., and Furlong, R. E.: Adelphi Hosp. Bull. 15:2 (May) 1957.
3. Foldes, F. F., and McNall, P. G.: Anesthesiology 13:287 (May) 1952.

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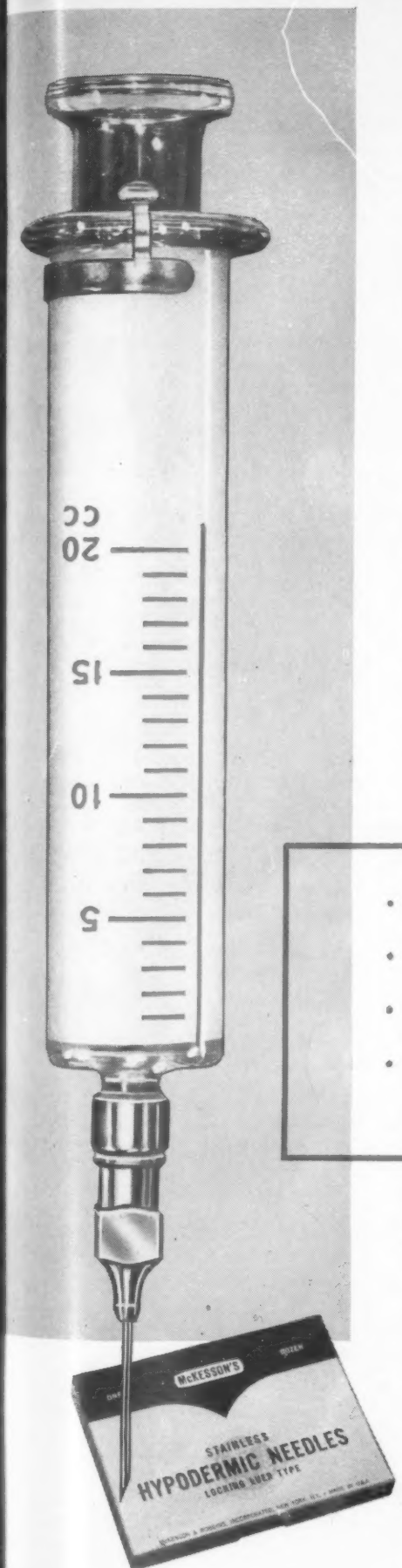

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whom the use of corticotropin is not practical. In such trials cortisone or hydrocortisone may be given in doses of 50 mg. every four hours and prednisone or prednisolone in doses of 15 mg. every four hours until pain is relieved. When the adrenocortical steroids or their analogs are used, the maintenance dosage of colchicine should be given concomitantly in amounts of 1.5 to 2 mg. daily.

The choice of an agent in the treatment of the acute attack will depend on the individual situation of the patient and on the presence or absence of associated conditions. Colchicine undoubtedly continues to be the drug of choice in handling the majority of patients. Its safety lies in the fact that the toxic effects are promptly recognized by the patient and use of the drug is discontinued. Its specific effect in gout is often of diagnostic aid; phenylbutazone and the hormones will also have suppressive effects on conditions closely resembling gout. Patients may be educated in the use of colchicine, beginning administration of the drug at the earliest sign of an impending attack. There need be no undue concern with the danger of self-medication. However, patients should be warned to keep the drug out of the reach of children because of its extremely poisonous effect when accidentally ingested. Phenylbutazone has the ability to stop the acute attack without the gastrointestinal disturbances that usually accompany the successful use of colchicine in a well-developed attack, but its toxic effects are more serious and are less likely to be apparent to the patient. Therefore, its use is preferably restricted to those patients who can be kept under close observation. Corticotropin therapy is usually practical only in those patients who may require hospitalization. It is particularly useful in severe attacks, in polycyclic attacks, and in patients who respond incompletely or only temporarily to colchicine. Both corticotropin and phenylbutazone therapy should be avoided in patients with complicating conditions, such as heart disease, in which the effect on sodium and water retention may be disastrous. A history of peptic ulcer is also a relative contraindication for their use.

General measures useful during an acute attack of gout are relatively simple. Bed rest is indicated if the attack is severe or if weight-bearing joints are involved, and the affected joints should be protected by a cradle for the bedclothes, with a splint or sling if necessary. Dietary measures are not effective in the treatment of an acute attack; usually a soft diet relatively high in carbohydrate is advised. A liberal fluid intake should be maintained. Salicylates or, if necessary, codeine may be used to control the severe pain until the effect from more specific measures is obtained. It is important that use of the joints should not be resumed too early during the subsiding stages of an acute attack. Weight-bearing joints should be protected by the use of crutches until all tenderness and swelling, as well as the pain, have subsided.

Interval Treatment

The objectives in the management of the intercritical period are twofold: to prevent subsequent acute attacks and to prevent or treat the deformities and disabilities of chronic tophaceous gout by inducing negative urate balance.

Prevention of Acute Attacks.—The most effective medication for prevention of acute attacks is the uninterrupted use of colchicine in doses of 0.5 to 2 mg. daily. The number of patients with gout who have taken colchicine daily for a decade or more is sufficiently large to indicate with assurance that such a regimen has been beneficial. Tolerance to the drug does not develop. Most patients will be able to tolerate 1.5 mg. per day in divided doses. Occasionally, some patients cannot take more than 1 mg. daily, whereas others will tolerate 2 mg. per day. Maintenance dosage should be given to all patients for at least three weeks after acute attacks and also during periods when factors that may precipitate acute gout are operative, such as acute infections, surgery, blood loss, emotional upsets, unusual exposure, or use of therapeutic agents such as liver extract and mercurial diuretics. Major or minor surgery should be preceded by at least three days of maintenance therapy, which should be continued for at least one week after the operation. The maintenance dosage of colchicine should be used indefinitely in patients having several attacks per year or in patients with evidence of chronic gouty arthritis. In milder cases, the maintenance program may be adjusted to the experience of the individual patient and put into effect during periods of high seasonal incidence, unusual work load, or other precipitating factors. Furthermore, all patients should be encouraged to recognize prodromal symptoms of an attack, such as diuresis, constipation, or unusual mood swings, and to increase colchicine dosage for one to two days in an effort to abort such attacks. They should also be advised to begin intensive colchicine treatment when the first symptoms representing acute articular involvement occur, rather than to wait for the attack to become fully developed.

The patient's history and experience should be carefully reviewed in an attempt to determine what precipitating factors are applicable to his individual problem. Insofar as possible, such precipitating factors should be minimized or eliminated. There is little scientific evidence that diet is an important factor in reducing the incidence of acute attacks, aside from the rare case of a patient in whom food allergy appears to be a trigger mechanism. Since many patients with gout are overweight, moderate caloric restriction with gradual weight reduction is indicated. Fasting or a sudden change to very low caloric diets may precipitate acute attacks. Moderate use of alcoholic beverages is permitted unless it clearly tends to induce acute attacks or unless there is impaired liver function.

Measures to Induce Negative Urate Balance.—Measures to induce negative urate balance consist of dietary restriction to limit exogenous precursors of uric acid and the use of a urate eliminant to increase renal excretion of uric acid. Recent studies indicate that the effectiveness of dietary restriction is definitely limited as a means of achieving negative urate balance. The availability of effective urate eliminants that can be administered safely over long periods of time permits a more consistent and greater reduction of the urates accumulated in the body than can be obtained by dietary restriction alone.

Exogenous sources of uric acid can be decreased by eliminating foods high in preformed purines, such as meat extracts, sweetbreads, liver, kidneys, anchovies, and smoked meats. In the majority of patients with gout, further dietary restriction does not seem justified. It has been clearly demonstrated by tracer studies that purines are synthesized in the body from the precursors of glycine, formic acid, carbon dioxide, and ammonia. Because of this lively biosynthesis of uric acid from the simplest precursors derived from virtually every foodstuff, the usefulness of dietary regulation

as a means of suppressing endogenous urate production is of necessity limited. Preliminary evidence, however, shows that purine biosynthesis may be accelerated in both normal and gouty subjects by a high protein intake. Therefore, in patients with severe gout, a further restriction of purine intake and limitation of protein to 50 or 75 Gm. a day, taken, insofar as possible, in the form of plant and dairy product protein, may be indicated.

Urate eliminants are used primarily to achieve negative urate balance and hence to prevent or decrease urate deposition in the tissues. Their effect in reducing the serum urate level is a good index of the extent to which the reduction of the body pool of urates has been achieved.

Probenecid, a potent urate eliminant of low toxicity, increases the urinary excretion of urates by a highly selective inhibition of the resorption of urates from the renal tubule. This results in an increase of urate excretion in the urine from 30 to 200% above base-line levels. This increase in excretion is often not maintained after the first few weeks of probenecid administration, but the increase in urate clearance and depression of serum urate levels persist as long as the drug is administered. The decrease in hyperuricemia is accompanied by a decrease in the size of the "miscible" urate pool and in increased rate of urate turnover. Prolonged administration of the drug can reduce the serum urate level, often to normal; it can minimize the deposition of urates in the tissue and decrease the size of established tophi.

The drug is administered in dosages of 0.5 to 1 Gm. twice daily. Treatment is usually initiated with a dosage of 0.5 Gm. twice daily, and, if serum urate level has not been restored to normal after two weeks, the dosage is increased to 1 Gm. twice daily. Since the effect lasts only as long as the drug is taken, patients who are receiving probenecid should be advised to take this medicament indefinitely. Some patients may experience acute attacks of gout soon after the initiation of probenecid therapy; therefore, it is wise to place all patients on maintenance dosages of colchicine prior to and during probenecid administration. Probenecid has no effect in the treatment of individual acute gouty attacks. There is usually no decrease in the frequency of attacks during the first few months after administration of this drug; however, in patients who have been on probenecid therapy for one to two years, there often is a decrease in the frequency and severity of the acute attacks.

The effect of probenecid is completely nullified during the administration of acetylsalicylic acid (aspirin) or other salicylates. Toxic manifestations to probenecid are infrequent and usually not serious. Occasionally, drug rash and gastrointestinal disturbances have been noted, and two serious anaphylactic reactions have been reported. Renal colic and urate calculi may occur during administration of this or any other urate eliminant, but this danger can be minimized by regulation of dosage and by maintenance of a high urine volume.

Some workers advocate the use of probenecid in all stages of gout as soon as the diagnosis is established. However, the clinical course of gout is extremely unpredictable, and the recommendation of prolonged medication to the patient who has had only a few acute attacks and who presents only a mild degree of hyperuricemia may be questioned. From the practical point of view, if such advice is given, it is rarely followed. This drug is clearly indicated in patients with

osseous or soft tissue tophi or with chronic gouty arthritis and also in those patients who, because of the clinical course or a sustained degree of hyperuricemia, appear to be candidates for development of these complications. At times it also seems worthwhile to add probenecid therapy to the program of patients with frequent acute attacks of gout, in the hope that after months of its administration the frequency of such attacks may be lessened.

Other drugs have definite urate-eliminant effects, but they possess other qualities that make them less desirable for prolonged use as therapeutic agents. Large doses of salicylates will definitely increase the uric acid excretion and decrease the serum urate level, but the dosage required for such prolonged action ranges from 6 to 9 Gm. per day. Few patients will tolerate such doses for very long. Phenylbutazone also has a definite urate-eliminant action when the plasma level of this drug exceeds 10 mg. per 100 cc. Relatively large doses are required to attain such a plasma level. Because of the toxic potentialities of this drug, its long-term use is not recommended when the desired results can be obtained by safer medication.

Treatment of Chronic Gouty Arthritis

The first step in the management of chronic gouty arthritis is to control the inflammatory involvement, which really represents a prolonged, continuous, or polycyclic acute attack. If relief cannot be obtained with colchicine, short courses of treatment with corticotropin in doses of 100 U. S. P. units per day, gradually tapering off over a total period of 10 to 14 days, may be helpful in unusually severe cases. Similar short courses with phenylbutazone in doses of 0.2 Gm. three or four times a day are also effective.

As the inflammatory element comes under control, the patient should be placed on the maintenance dosage of colchicine described previously. Probenecid should be introduced to obtain its long-range effect. Physical medicine and the application of orthopedic principles have much to offer the patient with severe crippling gouty arthritis. The exact methods used should be adapted to the general conditions of the patient and to localized joint involvement.

Surgery has a definite place in the treatment of chronic gout. Tophi should be excised if they become troublesome because of size, location in areas exposed to trauma, interference with joint function, or the development of discharging sinuses. Extensive involvement of the bones of the fingers and toes may require amputation.

Summary

Advances in the methods of treatment of gout permit effective control of the acute attacks and offer real hope that the advanced stages and late complications of gout can be prevented. Several effective methods are available for the treatment of acute attacks. Oral administration of colchicine remains the treatment of choice in the great majority of patients. Its successful use is dependent on promptness of instituting treatment, adequacy of dosage, and proper timing of the doses. Alternative reliable and effective methods in the relief of acute gout are intravenous administration of colchicine, oral administration of phenylbutazone, and the combination of corticotropin given parenterally with maintenance doses of colchicine. The use of urate eliminants such as probenecid has no effect on acute attacks.

Treatment between attacks has the twofold objective: to decrease the frequency of recurrent acute attacks and to prevent or treat the deformities and disabilities of chronic tophaceous gout by inducing negative urate balance. A maintenance dosage of colchicine given orally is the most effective medication in reducing the incidence of recurrent acute attacks. Dietary restriction of food containing preformed purines is helpful in obtaining a limited degree of negative balance, but a much greater effect can be obtained with administration of urate eliminants. The use of urate eliminants is helpful in the treatment of tophaceous gout and is definitely of value in preventing the development of the advanced stages of the disease.

It is important that the program of management be adapted to the individual patient and that it be varied according to the stage of the disease.

The Rackham Arthritis Research Unit is supported by a grant from the Horace H. Rackham School of Graduate studies.

J. Am. Med. Assoc. *164*:1670 (Aug. 10) 1957.

Council on Foods and Nutrition and Council on Drugs Report to the Councils

The Council on Foods and Nutrition and the Council on Drugs have authorized publication of the following report.

PHILIP L. WHITE, Sc.D., *Secretary, Council on Foods and Nutrition.*

HAROLD D. KAUTZ, M.D., *Secretary, Council on Drugs.*

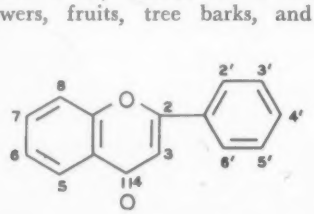
Flavonoids In Human Nutrition and Medicine

WILLIAM N. PEARSON, PH.D., NASHVILLE, TENN.

The recent upsurge of interest in the flavonoids, particularly in the use of these compounds in the treatment of numerous clinical disorders, has prompted the compilation of this review. No attempt has been made to be all-inclusive; rather, the review concentrates on a few well-documented findings derived from animal studies for use in the interpretation of the more controversial, less rigidly designed therapeutic reports. An excellent detailed review of several aspects of the subject of flavonoids has recently appeared.[1]

Chemistry

The flavonoids are carbon-hydrogen-oxygen compounds that are widely distributed in nature as pigments in flowers, fruits, tree barks, and vegetables.



The most important commercial source of these compounds is citrus rind. Structurally, the flavone nucleus consists of a benzenoid ring fused to a γ-pyrone moiety. A second benzenoid ring is attached to the carbon adjacent to the ring oxygen of the pyrone (see figure). Naturally occurring flavonoids contain hydroxyl or substituted hydroxyl groups, usually in the 3, 5, 7 and 2′, 3′, 4′ positions. Also, these compounds frequently exist as glycosides with the sugar (ordinarily rhamnose or rhamnoglucose) attached at the 3 or 7 position. Important compounds are the flavonols (hydroxyl group replacement of hydrogen in the flavone nucleus), flavanones (reduction of the 2:3 double bond), flavanols (hydroxyl substitution, reduction at the 4 position, and reduction of the 2:3 double bond), and the isoflavones (benzenoid ring attachment to carbon 3 instead of carbon 2).

From the division of nutrition of the departments of biochemistry and medicine, Vanderbilt University School of Medicine.

Toxicity

As one might expect from their occurrence in common plant foodstuffs, the flavonoids have a very low order of toxicity when taken orally. Subcutaneous and intraperitoneal injections of many flavonoids in relatively large amounts have also indicated a very low toxicity.

Nutritional Significance

Considerable interest in the possible nutritional significance of these compounds was aroused and championed by the reports of Szent-Györgyi and his coworkers[2] in the late 1930's. These investigators isolated a material from the peels of citrus fruits that they called "citrin" and reported it to be effective in decreasing capillary permeability in man. They also reported that scorbutic guinea pigs fed "citrin" not only outlived but had fewer tissue hemorrhages than their controls. Thus it was concluded that scurvy, as then produced in the guinea pig, was due not only to a deficiency of ascorbic acid but also to a lack of the "Permeabilitäts-Vitamin" (Vitamin P) as well. Shortly thereafter it was reported that the major ingredient in "citrin" was the flavanone, hesperidin; hence the implication that the flavonoids were of a vitamin nature. It soon developed, however, that these findings could not be duplicated in other laboratories, and in 1938 Szent-Györgyi reported that he could not completely confirm his earlier experiments. Likewise, the relatively recent reports of Scarborough,[3] who claimed to have produced vitamin P deficiency in two individuals, have not been confirmed.

As the matter now stands, there is no convincing evidence that any member of the flavonoid series is a required dietary nutrient for any known species. This was recognized in 1950 when the Joint Committee on Biochemical Nomenclature of the American Society of Biological Chemists and the American Institute of Nutrition recommended that the term "Vitamin P" no longer be employed.[4] No findings have appeared since then that would necessitate revision of this recommendation. In recent years, the term "bioflavonoid" has come to replace the term "Vitamin P." The latter, however, still frequently appears in the literature.

Effects on Capillary Fragility and Permeability

Because the original reports of the Szent-Györgyi group claimed that flavonoids were capable of decreasing capillary fragility in the human, a large percentage of the therapeutic studies of flavonoids deals with disease conditions that supposedly predispose the body to increased capillary fragility. The techniques employed in these studies deserve some scrutiny.

Fragility (the amount of resistance of the walls of a vessel to rupture and the ensuing leakage of red blood cells into the tissue spaces) has been routinely measured by applying negative or positive pressures to the skin areas for various periods of time and then

counting the petechiae, if any. Changes in wall permeability (the property of the vessel wall that permits passage of water and solutes) have usually been studied by measuring the rate of movement of certain dyes across the capillary wall into the adjacent tissues.

The validity of the techniques used in estimating fragility has been questioned. It has been shown in the human that the correlation between the positive and negative pressure techniques for measuring vessel fragility is low; furthermore, the reproducibility of results using either technique is unsatisfactory.[5] The method used for the measurement of permeability is somewhat more reliable. Nevertheless, the interpretation of results dealing with apparent changes in capillary fragility or permeability is not simple, since such changes can be the result of any one or several of a number of hemodynamic factors. For example, apparent changes in fragility or permeability may arise from changes in the structure of the vessel wall, from changes in blood volume, or from alterations in blood pressure.

Although a favorable effect of flavonoids on capillary fragility and permeability in man has not been convincingly established, there is some evidence from animal studies that such an effect might be possible. For example, it has been found that certain of the flavonoids have antioxidant activity in vitro (and possibly in vivo) toward both ascorbic acid and epinephrine. The protective effect of flavonoids against the copper-catalyzed autoxidation of epinephrine in vitro has been postulated as being due to copper chelation by the flavonoid or to formation of a flavonoid-epinephrine complex with the flavonoid then being preferentially destroyed.[6] It is possible that these antioxidant properties may partially explain the pseudovitamin effects noted by the early workers, but similar studies of the influence of flavonoids on ascorbic acid autoxidation do not appear to have been carried out. A definitive study is needed to clarify the physiological relationship, if any, between flavonoids and ascorbic acid.

Ambrose and DeEds[7] have proposed that the epinephrine-protective action of the flavonoids may explain their findings in the influence of flavonoids on vascular permeability in the guinea pig. These workers studied the visualization of trypan blue in shaved, chloroform-irritated skin areas of rabbits before and after the intravenous injection of rutin. This flavonoid appreciably increased the time required for visualization of the dye. Similar findings were recorded by Bohr and associates[8] in studies of the guinea pig, in which Evans blue dye was used. It is suggested that the flavonoids may prevent the destruction of epinephrine, with a resulting potentiation of vasoconstriction and subsequent decrease in capillary blood flow. Further insight into this question has been provided by Schiller,[9] who quantitated, by photometric means, the transport of fluorescein from capillaries into adjacent areas when rutin or ascorbic acid was introduced intravenously. The effects of injecting epinephrine and arterenol (nor-epinephrine) at the site of the fluorescence readings in the presence and absence of an adrenergic blocking agent, phenoxybenzamine hydrochloride (Dibenzyline), were also recorded. The delay of the transport of fluorescein produced by administration of rutin, even in the presence of phenoxybenzamine, may be interpreted as evidence that rutin not only prolonged the action of epinephrine (prevented autoxidation) but had an independent vasoconstrictor action as well. Additional evidence has been presented for an indepedent vasoconstrictor action of flavonoids by these and other workers.[10] It should be emphasized that these are not unique pharmacological properties and that they are rather weak when compared to those of other available agents.

By extrapolation from these animal studies, present knowledge of flavonoids in this area may be summarized by stating that if flavonoids affect capillary fragility and permeability in man, they may do so because they possess certain pharmacological properties and not because they are normally involved metabolically or structurally in maintaining the integrity of the vessel wall.

Effects on the Common Cold

Several brief clinical reports have been published, claiming that flavonoids have a remarkably favorable influence on common respiratory infections by virtue of their supposed capacity to increase capillary resistance. Recently, considerable publicity has been given to the use of these substances in the treatment of the common cold, and several "cold" preparations containing flavonoids have actually appeared on the market. The best clinical studies of this claim have appeared recently in THE JOURNAL. Franz and coworkers[11] carried out a controlled study on 89 individuals. Placebos, flavonoid plus ascorbic acid, ascorbic acid alone, and flavonoid alone were administered to four groups for a period of three months. Neither the subjects nor the examiners knew the content of the capsules taken. From the findings, it was concluded that flavonoids affected neither the incidence or cure of colds nor the ascorbic acid levels of the blood serum.

The detailed report of Tebrock and associates[12] is probably the most definitive clinical report in the flavonoid literature and may serve as an example for those who are engaged in evaluating the clinical effects of drugs. These workers studied the effects of placebos, flavonoid plus ascorbic acid, flavonoid alone, and ascorbic acid alone, in combination with a standard palliative preparation, on colds occurring in nearly 2,000 persons. Neither the patients nor the examining physicians knew the identity of the administered medicament. In the opinion of the investigators, there is a singular lack of effect of both flavonoids and ascorbic acid in altering the course of the common cold. In no instance did apparent differences reach the 1% level of significance, and, in most cases, simple inspection of the data is sufficient to deny significance.

These results contrast sharply with those of Macon,[13] who reported a high rate of relief of cold symptoms in 121 patients (74.2%) on the second day of treatment with capsules containing 100 mg. of flavonate glycoside, 50 mg. of ascorbic acid, and 226.8 to 291.6 mg. of acetylsalicylic acid. This worker also noted a 50.9% improvement with the "control" preparation which contained 84.24 mg. of acetylsalicylic acid, 64.8 mg. of acetophenetidin, and 12.96 mg. of caffeine. Since this preparation was not a true control (that is, quantitatively and qualitatively similar except for one ingredient), the apparent 23.3% superiority of the test preparation cannot be properly regarded as due to its bioflavonoid content. Furthermore, in assessing the results of a study of this sort, it is important that individual bias be held to a minimum. It is not possible to determine from the limited data presented in this paper how well this was accomplished. For example, it is not clear how many examiners were involved or

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whether the patient or examining physician knew the type of medicament being given. However, a study encompassing 1,831 workers is still in progress and will be the subject of an extended report. It is hoped that the publication of this study will answer the questions that arise in connection with the initial report and will be presented in a fashion susceptible to statistical interpretation. On the basis of the best evidence now at hand, it would appear that flavonoids have no significant effect, palliative or otherwise, on the course of the common cold.

Other Clinical Applications

The effects of flavonoids on such clinical entities as hypertension, diabetes, rheumatic fever, arthritis, and pregnancy have been studied. In addition, flavonoids have been used in the treatment of nonthrombocyctopenic purpura, vascular purpura, allergic purpura, idiopathic thrombocytopenic purpura, and hereditary hemorrhagic telangiectasis. It is not possible to reach a valid conclusion as to the efficacy of flavonoid treatment in these conditions because of (1) the general unreliability of the techniques employed, (2) the absence of double-blind placebo controls, and (3) the spontaneous remissions that are known to occur during the course of many of these conditions. Although it is admittedly difficult to obtain ideal experimental conditions in clinical situations, the therapeutic studies of the flavonoids seem to suffer peculiarly from lack of proper design. It is also likely that the reluctance of individuals to publish negative findings has resulted in a more favorable literature than is deserving.

Absorption and Metabolism

Evidence concerning the absorption and metabolism of the flavonoids is incomplete and somewhat contradictory, but it is encouraging to see that some work is at last in progress along these lines. Apparently the most thorough investigations in this area have been carried out by Murray and co-workers.[14] This group has recently presented evidence that metabolites of flavonoids were excreted in the urine of the rabbit and rat after oral administration of flavonoids. After the feeding of rutin or quercetin, homovanillic acid, 3-hydroxyphenylacetic acid, and 3,4-dihydroxyphenylacetic acid were found. Of these, the last compound accounted for some 25% of the quercitin fed. It was also reported that administration of either hesperidin or homoeriodictyol resulted in urinary excretion of 3-hydroxyphenylpropionic acid by the rabbit. Administration of homoeriodictyol also gave rise to dihydroferulic acid, and the feeding of naringenin resulted in the excretion of 4-hydroxyphenylpropionic acid. It is also stated in this report that a conjugate of unspecified nature of the parent substance administered was excreted.

Physiological and Pharmacological Functions

In addition to their supposed vascular functions, numerous other physiological or pharmacological functions have been proposed for the flavonoids, but few have stood the test of time. For example, reports that the phosphorylated flavonoids are antifertility factors remain unconfirmed, and claims that certain flavonoids and their derivatives are involved in the sexual process of algae have been denied. Only one other function of the flavonoids seems to be sufficiently documented and clear to warrant recognition: Certain of the isoflavones present in clover, alfalfa hay, and soybean meal are estrogenic. However, the relatively low potency of these compounds (1/50,000 that of diethylstilbestrol) suggests that they may not account for all of the estrogenic activity of subterranean clover, the consumption of which has been found to lead to a reproductive disturbance in sheep.[15]

Summary

The high hopes once held for the flavonoids as important metabolites have not materialized. Instead, present knowledge indicates that, while they possess mild pharmacological properties under certain conditions, the flavonoids have no known nutritional functions. They cannot be regarded as essential nutrients. Those workers who claim therapeutic value for the flavonoids have not supported their claims with data obtained from well-controlled clinical studies. Until such studies are made, it must be concluded that the flavonoids are of little or no value in the treatment of disease.

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Barnstead Briefs

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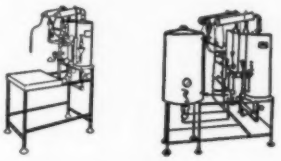

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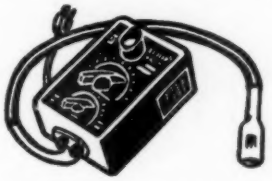

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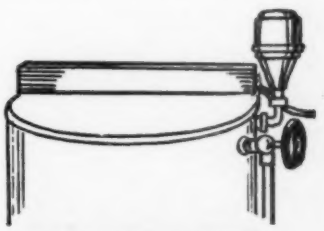

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LETTERS

Law Number Valuable

DEAR SIRS: Just a note of thanks and appreciation for your lucid and comprehensive article on "The Law of Hospital Pharmacy" in the May-June issue of THE BULLETIN. It will be of inestimable value in preparing our course in Hospital Pharmacy Administration and will be a constant reference for checking up on our everyday practices.

WILLIAM M. HELLER, PH.D.
Chief of Pharmacy Service
University of Arkansas Hospital
Little Rock, Arkansas

Interested in Reprint

DEAR SIRS: I would like to obtain a reprint of the article entitled "The Use of Antiseptic Impregnation of Fabrics in the Treatment and Prevention of Disease," by C. A. Lawrence and A. J. Maffia. This appeared in the March-April issue of THE BULLETIN.

L. S. HARTFORD, *Assistant Administrator of Hospitals.*
University of Texas—Medical Branch
Galveston, Texas

Compliments

DEAR SIRS: Thank you for accepting my application for membership in the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

As a member of the American Pharmaceutical Association since 1951, I am well aware of the work done by our national professional associations. To my way of thinking, a national association is the only way to understand one another in the profession and to further the cause of interprofessional relationships.

Again, thank you for the honor of membership and keep up the good work in our organization.

JOHN GILLEN
612 *Sixth Avenue*
New Hyde Park, New York

DEAR SIRS: I am a Chief Pharmacist in a private 400 bed teaching hospital. Recently I was asked by our administrator to teach pharmacology to the student nurses and would appreciate any help or information you might have on the subject.

Thanks for another year of very wonderful informative BULLETINS. Please keep up the good work.

GENE BLASI, *Chief Pharmacist*
Baptist Hospital Pharmacy
Louisville, Ky.

Good Public Relations

DEAR SIRS: I thought that it would be in the interest of Pharmacy to note that the Department of Pharmacy of Albany Hospital set up an exhibit in a booth at the Altamont Regional Fair, Altamont, N. Y. This is a tri-county fair which attracted 100,000 people. This is the first time in the history of this sixty-third annual regional fair that a Pharmacy exhibit was displayed.

The theme of the exhibit was "A Century of Progress 1857-1957." A display of equipment emphasizing these two periods was presented. I am enclosing a photograph for your consideration and publication.

Thank you for your interest and cooperation.

LOUIS P. JEFFREY, *Pharmacist-in-Chief*
Albany Hospital
Albany, New York

Pharmacy Exhibit sponsored by the Department of Pharmacy, Albany Hospital, Albany, N. Y. at the Altamont Regional Fair, Altamont, N. Y.

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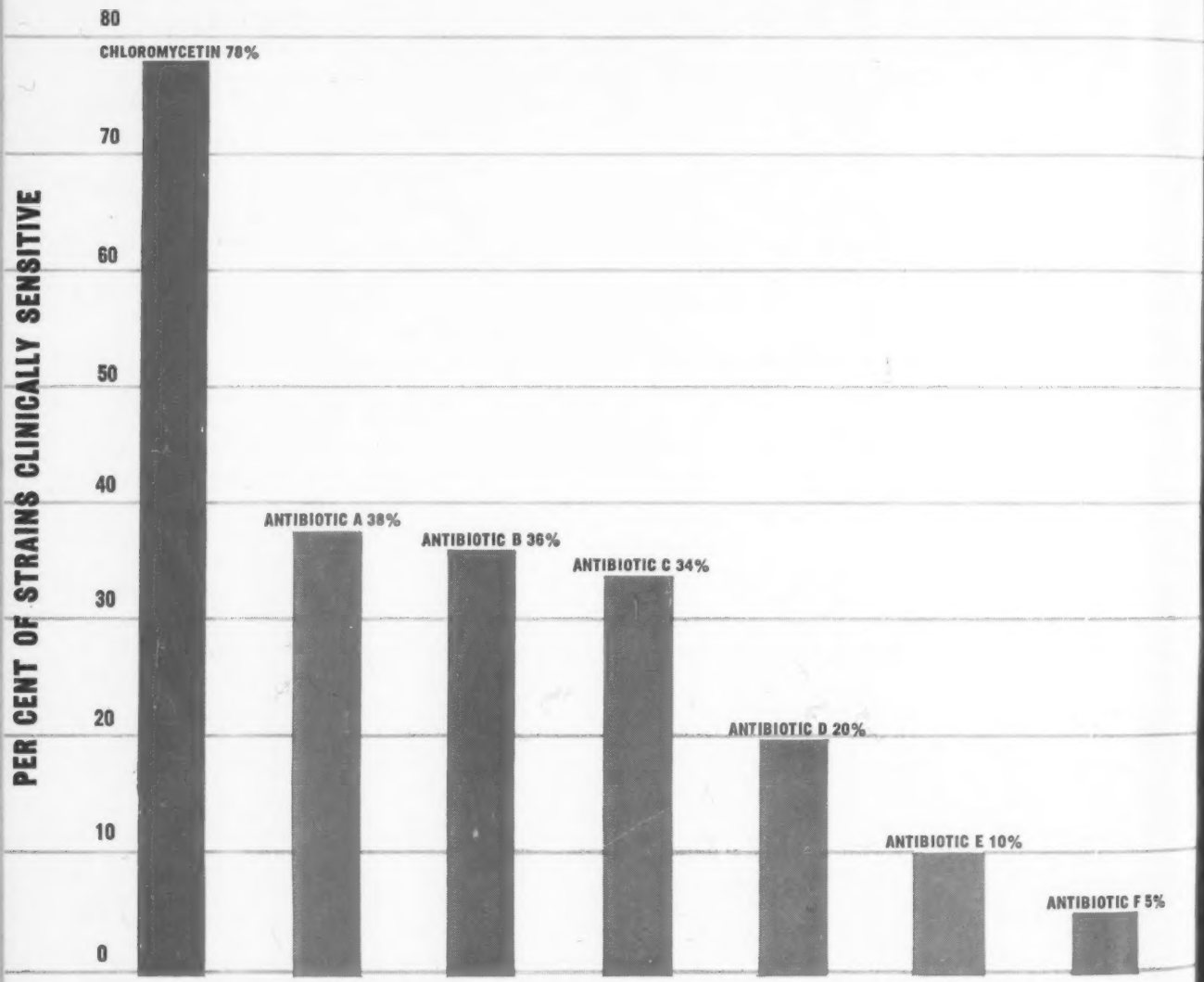

COMPARATIVE SENSITIVITY OF MIXED PROTEUS SPECIES TO CHLOROMYCETIN AND SIX OTHER WIDELY USED ANTIBIOTIC AGENTS*

*This graph is adapted from Waisbren, B. A., & Strelitzer, C. L.: *Arch. Int. Med.* 99:744, 1957. It represents *in vitro* data obtained with strains isolated from patients between the years 1951 and 1956. Inhibitory concentrations, ranging from 3 to 25 mcg. per ml., were selected on the basis of usual clinical sensitivity.

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EDITORIAL

Ten Guides For The Operation Of A Formulary System

by DON E. FRANCKE

Methods of operation of the formulary system differ somewhat from hospital to hospital. While this is inevitable, and in some respects desirable, there are still certain principles upon which the operation of the formulary system in all hospitals should be based. Some of these guiding principles may be stated as follows:

1. VIEW the formulary as a dynamic, ever changing compilation of modern pharmaceuticals selected with discrimination, not as a static, fixed, inflexible list of drugs and preparations.

2. MAINTAIN a formulary which reflects the clinical judgement of the hospital's medical staff and is a critical selection of those drugs that are considered most useful therapeutically together with the preparations whereby these drugs may be administered most effectively.

3. SUPPLY to each member of the medical staff clearly written policies and procedures governing the operation of the formulary system which have been formulated by the Pharmacy and Therapeutics Committee and approved by the medical staff and administrator.

4. DISPENSE the brand of drug prescribed on each individual prescription or contact the physician and obtain his permission each time before another brand of the drug is dispensed, if no written, approved policies relative to the operation of the formulary system exist.

5. AGREE to an *administrative* policy to dispense another brand of a drug in place of the drug prescribed *only* when that policy has been approved by the medical staff.

6. FORMULATE procedures for obtaining non-formulary drugs which are simple, fair and reasonable, and do not involve needless delays and complicated red tape.

7. STRIVE for a formulary system which will provide, in addition to drugs accepted into the formulary, for:
(a) The clinical evaluation of non-formulary drugs by members of the medical staff;
(b) The clinical evaluation of investigational drugs;
(c) the exercise of a physician's professional prerogative in instances when he believes a specific brand of a drug is important to the care of his patient.

8. REMEMBER that the pharmacist is responsible for " . . . specifications, both as to quality and source, for the purchase of all drugs, chemicals, biologicals and pharmaceutical preparations used in the treatment of patients . . . " according to the Minimum Standard for Pharmacies in Hospitals. This responsibility is inherent in the proper operation of a good formulary system.

9. KEEP the Pharmacy and Therapeutics Committee effective by a well-prepared, challenging and interesting agenda, by compiling and distributing background information on items to be discussed, by holding regular meetings, and by communicating the Committee's recommendations to the medical staff.

10. UTILIZE the Pharmacy and Therapeutics Committee, of which the pharmacist is an active, voting member, to establish and maintain good communications and liaison between the pharmacy and the medical staff in the interest of better patient care. Remember that the hospital pharmacist is a member of the health team that serves the patient.

A well-operated formulary system must be guided by principles which are just and fair to the patient, the medical staff, the pharmacy staff, and the hospital. Especially important is the spirit with which the system is operated. If the pharmacist, on whom falls the responsibility of implementing the formulary system, maintains an attitude of helpful cooperation with the medical staff, if he fosters the formulary system as an educational tool for practitioners and students of medicine, nursing and pharmacy, if he encourages the acceptance and use of really new and better drugs as they are developed and evaluated, and if he employs the formulary system to actively promote better patient care—if he does these things and is guided by sound professional principles, the formulary system in his hospital will be well accepted by all.

I HAVE ALWAYS HAD a very deep interest in that segment of our profession known as hospital pharmacy. All of you serving as hospital pharmacists are fortunate in having an opportunity to practice your profession in an ideal professional atmosphere with a close personal relationship with other members of the health professions.

In considering the subject assigned to me by your committee, "The Relationship Between the Pharmaceutical Industry and Hospital Pharmacy," I noted that Webster defines the word "relationship" as "the state of being mutually interested." It seems to me that this definition clearly defines

E. BURNS GEIGER is Director, Professional Relations, Pfizer Laboratories, Brooklyn, New York.

Presented at the Eighth Hospital Pharmacy Seminar, University of Texas, Austin, Texas, February 11, 1956.

RELATIONSHIP BETWEEN

the pharmaceutical industry and hospital pharmacy

by E. Burns Geiger

what I feel is the relationship between the pharmaceutical industry and hospital pharmacy.

Mutual Interests

The development of an organization or team of all the interested individuals tends to strengthen our mutual efforts and interests. You could liken the mutual interest between our two groups to that which is found in Texas when producing oil. The fact that an individual owns some land on which there is oil does not mean that the benefits of that oil can be brought to the public without team efforts on the part of the land owner, the drillers, the processors and those at the local level who supply the finished product to the consuming public.

This somewhat parallels the case of a member of industry, who, through research, develops a new drug product. However, the benefits of the product cannot be brought to the patient without assistance from a teammate from hospital pharmacy assisting in the clinical evaluation of the new product. It is also the responsibility of the hospital pharmacist to advise the professional staff of the availability of the new product, its method of use, and to dispense it to the patient. The end result of this team action is benefit to the patient.

Since we do have a mutual interest in (1) the profession of pharmacy, and (2) providing services of pharmacy for the welfare of the patients, we should establish a goal—an accomplishment toward which our team can strive.

I once read that the basic responsibility of the hospital is "making sick people well, and returning them to their every day life as normal, productive members of society." I can think of no other goal that offers as much of a challenge as the one we have in overcoming sickness and disease and in seeing a person in need of medical care receive the services of our team and return to his family and loved ones.

Since we do represent a team and therefore, should perform as efficiently as possible, each member must accept responsibility for his share of the total team effort. This can be done by effectively utilizing those inherent characteristics and acquired skills that qualify us as individual members of the team. In addition to assuming a share of the total responsibility, each person, of course, must be willing to assist his teammates.

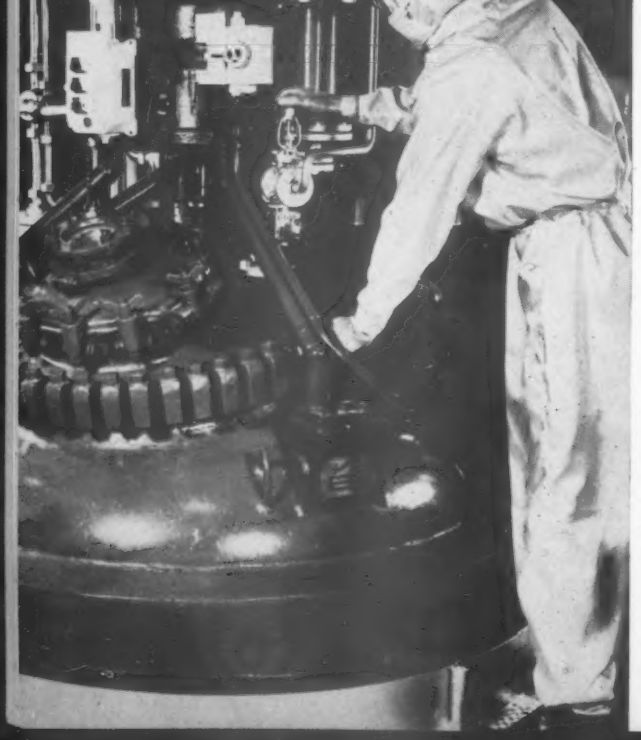
Let's look at the individual members of our team and determine what contribution each can make to the total effort. In surveying the team members from the pharmaceutical industry, and those from the hospital pharmacy, it is surprising how often we find qualifications and responsibilities common to both.

Basic Responsibilities

First, let's look at the basic responsibilities of each of the team members. The representative of industry, whether a hospital sales representative or the regular professional service representative, is responsible to the health professions, to his management, and to the public. The hospital pharmacist is responsible to the medical staff, to the patients, and to hospital administration for the efficient and economical operation of the pharmacy.

The representative of industry has research facilities devoted to developing new products, and the improvement of those products on the market. The hospital pharmacist plays a major role in that important phase of the development of new products known as "clinical evaluation." Those from industry have the manufacturing facilities for developing new products, whereas the hospital pharmacist dispenses these products and in many instances, modifies or prepares different dosage forms. The representative of industry has available the resources of his advertising department for developing special pieces of literature for use when detailing and contacting members of the health team. The hospital pharmacist, likewise, provides information to the medical staff. He may do this through his services on the

Crystallization Process—Technician of Chas. Pfizer & Co., Inc., adjusts valve on antibiotic crystallization tank in Groton, Conn.



Steps in the clarification of solutions

Pharmacy and Therapeutics Committee, by establishing a new drug section in the pharmacy, through memorandums to all members of the staff, with up to date information on the latest therapeutic advances, or by other methods. The manufacturer's representative has supporting him several types of special literature and other essential information for answering inquiries from physicians, pharmacists, and other professional contacts. The hospital pharmacist, through his services on the Pharmacy and Therapeutics Committee or from daily contacts, also obtains and provides similar information for members of the staff.

The representative of industry also has a number of special services, such as the laboratory advisory services which provide information on sensitivity of offending organisms and other information of interest to laboratory personnel. The hospital pharmacist, on the other hand, through a phone call or a personal visit down the corridor, can discuss problems of mutual interest related to these special services. I think you will find through a review of the parallel services each member of the team has to offer, that there is a great deal in common between the teammate from industry and the hospital pharmacist.

I believe all of you are aware that it is common practice in large organizations to have written descriptions listing the basic responsibilities of each position in the organization. In addition, the responsibilities are amplified in standards of performance. In reviewing the position description and standards of performance for hospital sales representatives working for Pfizer Laboratories, I was not too surprised to note that of the twenty basic elements listed, fourteen emphasized the representatives' responsibilities in the area of service to the customer. The other six elements outlined the representatives' responsibilities in selling. You might be interested in a review of some of these. The number one responsibility as listed in the position description, is "making regularly scheduled visits to hospitals." The second is "contacting all departments whose functions bear in any way on our business or professional relations." The third duty is "detailing professional personnel on our products." Number four—the first one, you will note which specifically mentions selling—reads "obtaining orders and assisting in emergency needs, and expediting shipments when indicated." Although major emphasis is placed on selling, there is also an element of team play. We emphasize that the representative should be of assistance to you

and the hospital in your emergency needs, or when expeditious shipments are necessary. These are examples of the general thinking in the pharmaceutical industry of supplementing our basic sales responsibilities with providing service to you and your associates in the hospital—service which can be useful in improving your care to the patient.

Several other responsibilities are worth mentioning. Let me quote just one or two of them for you. "The hospital sales representative is responsible for making recommendations for special literature." In other words, literature that would have particular appeal and important use in specialized hospital practice. The representative also, "provides teaching aides and other material to nursing and other professional personnel." Another responsibility which we have stressed is the importance of our representatives taking an active part in those collateral duties which you accept as necessary to improve your stature as a hospital pharmacist. It reads "The hospital sales representative will maintain an intimate knowledge, and where indicated, participate in activities related to hospital operations, such as hospital pharmacy societies and associations."

One of our representatives is assigned to each school or college of pharmacy in the United States. We trust that the services of these people can be utilized in some measure by those in the teaching profession who have the important responsibility of developing the future hospital pharmacists of the country.

This brief review of the standards of performance shows that we emphasize the "service" responsibilities of our representatives. The availability of these services, however, is only as effective as their utilization by you and the other hospital pharmacists.

In addition to the resposibilities we have outlined for our representatives, those at the management level also are attempting to recognize and help solve some of the problems of hospital pharmacy. Within the past six months, we have prepared a hospital sales reference manual. In this manual we have outlined those areas in dealing with hospitals which set this group somewhat apart from the others. Throughout the manual, we have cautioned the representatives to learn to know the hospital pharmacist, as well as all other personnel in the hospital. In addition, we have emphasized the need for complying with the local rules and regulations that have been established for the operation of the hospital.

All of the items in our manual receive continuous revision to keep them current and in conformity with the policies and practices in the majority of hospitals.

Advisory Committee

We have established a Pfizer Hospital Pharmacy Advisory Committee. This Committee is made up, at present, of thirteen hospital pharmacists from all areas of the United States. Meetings between this Committee and management personnel have made it possible to develop many of the aids I have mentioned earlier. The cooperation and spirit of participation by each of the members of the Committee in discussing and assisting us in resolving apparent problems in our relations with hospital pharmacy have been most encouraging. The establishment of this Committee somewhat parallels the services of a coach in improving team effort.

Under present plans, the Committee will be continued and we trust it will be possible to rotate membership so that we will have the counsel of hospital pharmacists from all areas of the country. In selecting the Committee, we have attempted to obtain hospital pharmacists from teaching hospitals, non-teaching hospitals, government activities, university affiliated hospitals, as well as both large and small institutions. We feel that from the experience gained by meeting with these people and discussing matters of mutual interest with them, we in industry will be able to learn to be better teammates for the hospital pharmacist.

Hospital Pharmacists' Role

I have reviewed for you some of the things that industry is doing. Let us now consider what members from industry expect of their teammates from hospital pharmacy. I think our expectations can be oversimplified in one or two sentences. All that we ask is the opportunity to discuss with you matters of mutual interest or concern. Also, we want to work closely with you as a true teammate in carrying out your basic responsibilities to your hospital staff. As is true in any team effort, the success of this effort will depend upon the development of the degree of mutual cooperation that makes any team effort effective.

I am aware of the responsibilities of each of these two groups. Although we do have similar responsibilities, we have others that cannot be as closely related. We are aware of your prime responsibility to your medical staff, your patients, and your administrative officials. We appreciate your responsibilities, and for that reason we attempt to regulate our operations to conform with these rules and regulations that have been

developed by you and other members of the hospital organization. At the same time, we know you appreciate that the representatives of industry who contact you, also have a responsibility to their management to make their existence economically feasible. We will make a winning team if we can remember that although we are teammates, we are still individuals. Although we have many common responsibilities, we also have others that can only be understood when discussion, understanding and cooperation take place between us.

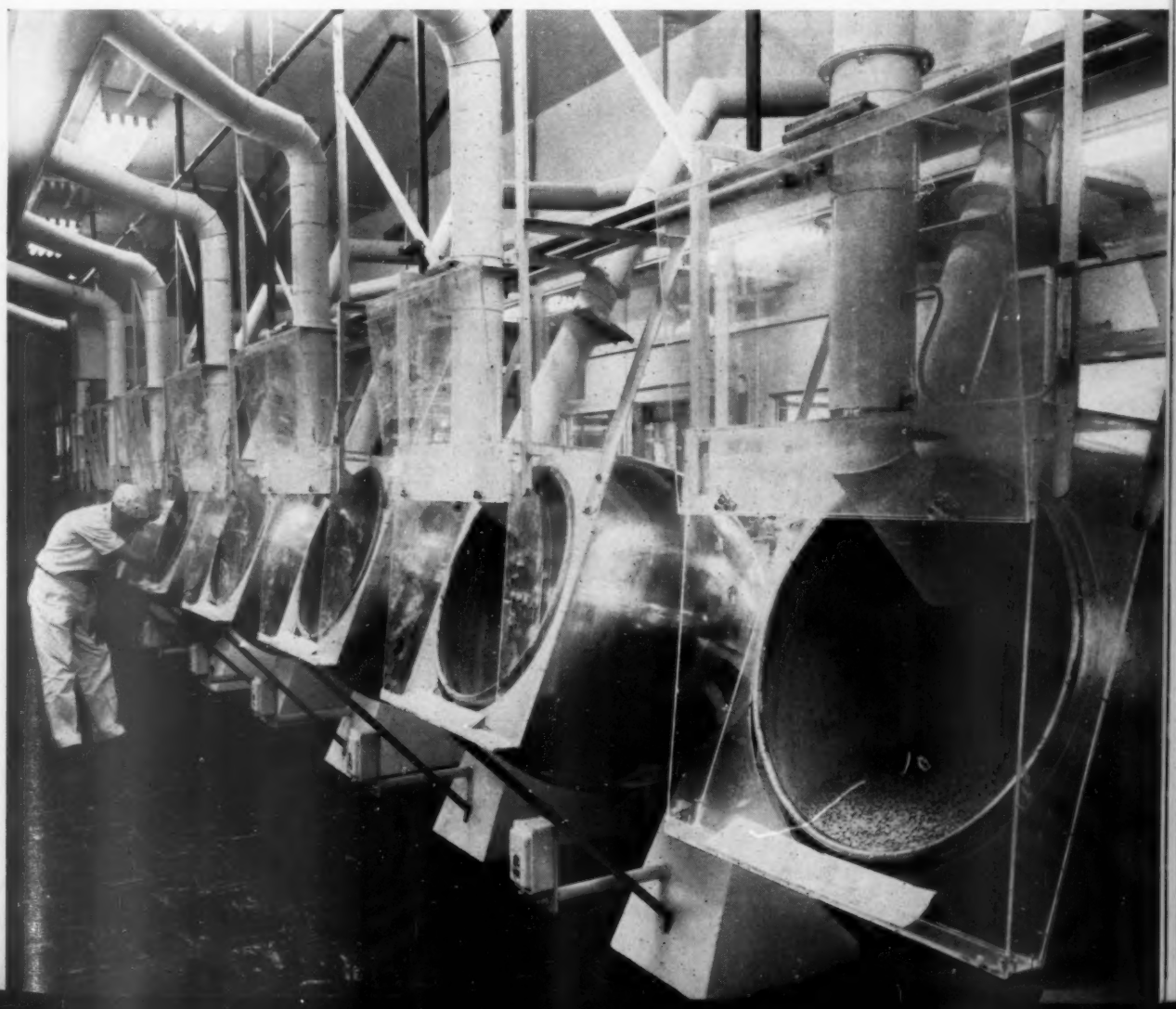
New Horizons

I am, by nature, an optimist and therefore can see a very bright future for not only hospital pharmacy but the entire profession. You hear the charge from some pharmacists that the trend toward the development of finished dosage forms by the manufacturer is reducing them to the status of "pill counters." It is my feeling that by having medication prefabricated, the pharmacist can then devote more time to those services that mark him as a true professional man. I am referring to the responsibility of pharmacists to serve as consultants to members of the other health professions, to keep them advised of the latest trends in therapy, the latest developments in drug items, dosages, indications, contraindications, and all of the information necessary when using the effective drug products we have at our disposal today.

I trust that my comments have not sounded too much like someone with his head in the clouds, or his eyes on a star. I feel quite strongly about the need for closer cooperation between all of the segments of pharmacy, so that this great profession of ours can continue to move forward in pace and parallel with the progress being made in the other health professions.

I agree with Webster that the relationship between the pharmaceutical industry and hospital pharmacy is a wedding of those with a mutual interest. That mutual interest is to provide the highest quality pharmaceutical products which are so necessary for returning our patients to normal productive lives.

Coating Tablets—Technician checks tablets in a row of large stainless steel coating pans in the Brooklyn, N. Y. plant of Chas. Pfizer & Co., Inc.



APPLYING *work simplification* TO HOSPITAL PHARMACY

by NORMAN N. BAKER

AN EFFICIENT PHARMACEUTICAL SERVICE in the hospital depends upon the utilization of time, motion, and the expenditure of energy by people.

The more efficiently a person's time, motion, and energy are used the greater the production and the greater the sense of work accomplishment and the happier and more stable the employee.

To study ways to increase our efficiency, then, let us examine the use of our time, motion and energy.

No other group of people are more conscious of time than those who work in hospitals. Too often, however, we hurry at our tasks adopting slipshod ways, decreasing our efficiency, and lowering our output. Time is lost principally through poor planning, poor instruction, poor equipment, and procrastination. The application of work simplification will promote the better utilization of time.

Normal Work Areas

There are few jobs in the hospital that can be accomplished without motion. If we conserve motion, we save time and energy. We must apply principles of motion economy by arranging the work area and prepositioning the equipment so that the motions of the physical activity involved will be simple, smooth, rhythmic, and productive. A chart giving specifications on normal work areas has been distributed for your study.

The best way of doing a particular job is not the best way until the worker is convinced, through simplification of the job and subsequent training, that he can do the job easier and as well.

NORMAN N. BAKER is Apothecary-in-Chief of The New York Hospital, New York City.

Presented at the Annual Convention of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS at New York City, April 29, 1957.

to simplify work—

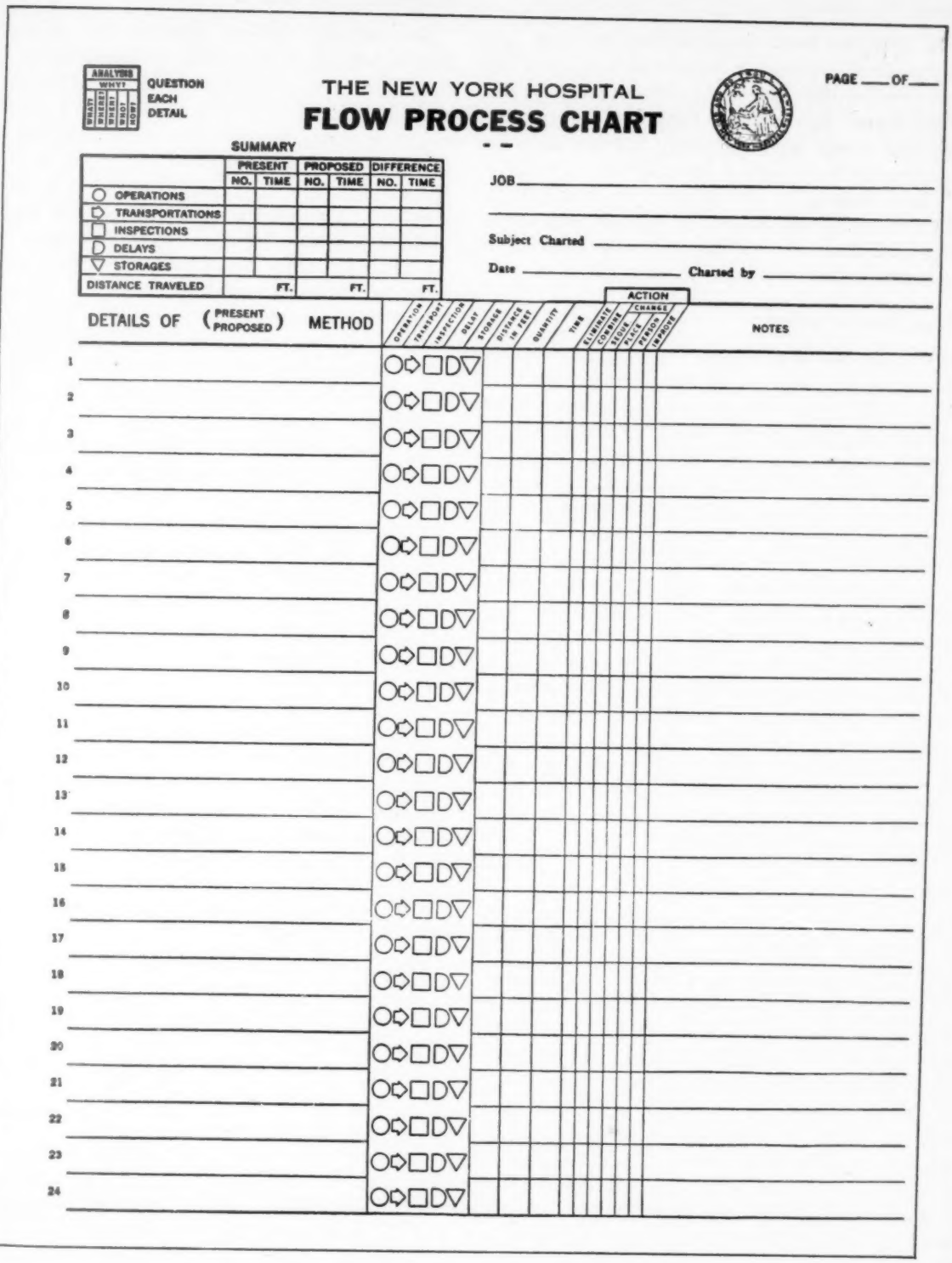
1. Pick a job to improve.
   Look for jobs giving trouble.

2. Make a flow process chart.
   List every detail.

3. Challenge each detail.
   WHAT is its purpose?
   WHY is it necessary?
   WHERE should it be done?
   WHEN should it be done?
   WHO should do it?
   HOW should it be done?

4. Work out a better method.
   ELIMINATE unnecessary details.
   COMBINE details when practical.
   CHANGE for a better sequence.
   IMPROVE all necessary details.

5. Apply the new method.
   Use it until a better method is developed.



By looking at the way our workers do their work and conserving their time and motion, we will conserve their energy and the efficiency of a more contented worker will be our reward.

The basic idea of work simplification is not new, but the part that is new is the organized application of common sense in a manner which has been designed and streamlined for use in daily problems. Its principle is not one of speed-up, but one of appeal to the personal selfishness of every person who would like to do his job in an easier and better way.

Select The Job

In applying work simplification we must first pick a job to improve; a bottleneck job, a job that takes a lot of time, our time; like the job requiring many materials, tools and supplies; the prepackaging of drugs for dispensing; the processing of inpatient and outpatient prescriptions, the filling of drug baskets, or the delivery of drug baskets. If we sincerely feel that we have a job that can be improved then we are on our way toward the successful application of work simplification.

Flow Process Chart

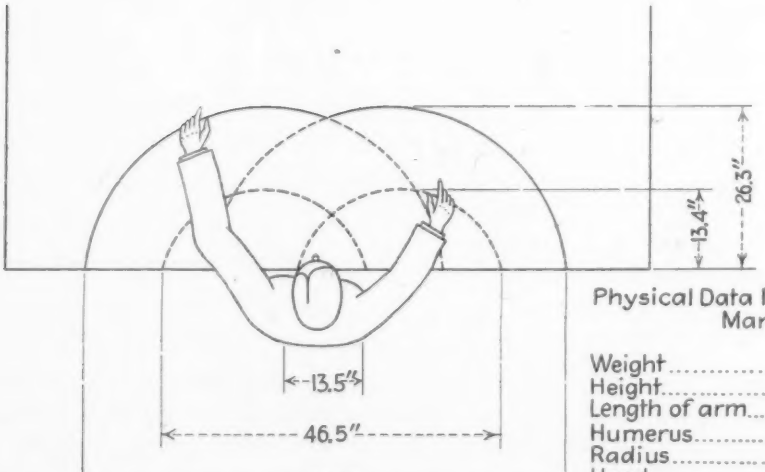
To improve any job we must first know how the job is presently being done. One way to do this would be to take a moving picture of the procedure from the beginning to the end, then slow the picture down and look for wasted motion, unnecessary steps and time-consuming operations. The heavy hand of operating budgets however would prevent most of us from obtaining a movie camera, so instead we use the most valuable of all the work simplification tools—the Flow Process Chart. The completion of this chart, then, is the second step in the improvement of any job. Upon examination of the chart you will note that it permits a graphic representation of the sequence of events in any process or procedure and includes information organized in such a manner as to permit subsequent analysis. The principle of the flow process chart has been applied in many phases of industrial management work and its value has been definitely proven.

Analyzing The Job

In analyzing a job we must see everything, and that is why it is impossible to complete a flow process chart while sitting at a desk. After picking a specific job or activity for study, we choose the object or person to follow, remembering that each detail followed and recorded must pertain to the specific job chosen. We must establish a starting and ending point for the job to insure that we cover the ground we desire and no more. Then we record a brief description of each detail of every operation, step by step no matter how short, trivial or temporary; every operation, every move, every storage and every inspection must be recorded. This is the secret of the flow process chart; for to list every detail of a job is to see that job as it is actually being done.

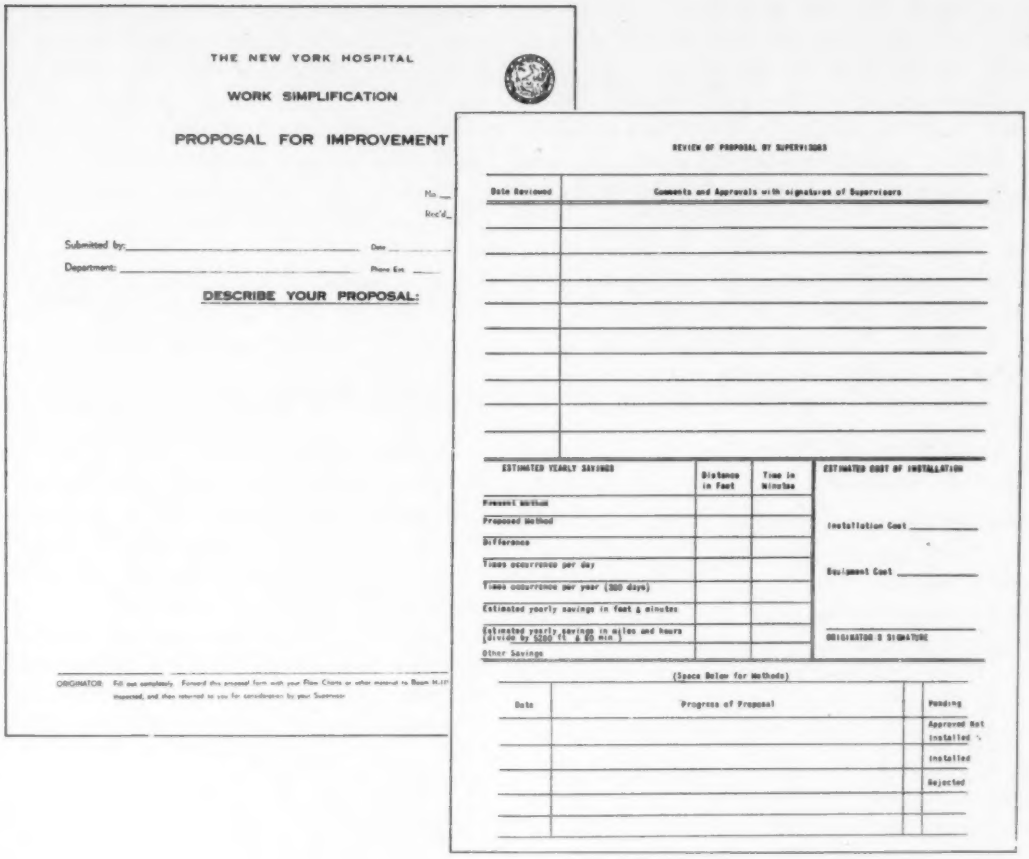
Every detail recorded is identified by one of the symbols in the center column of the chart, and a connecting line is drawn between each of the proper symbols describing the method or job. As every job can be broken down into three major components; the make-ready, the do, and the put-away operation; we block in or darken all the symbols representing "do" operations. The "do" operation represents the actual work done. It is that part of the whole job or procedure for which the employee is obtained. The make-ready operation is the effort and time that goes into setting up equipment and obtaining material to work with. The put-away operation is the clean up in order to make ready for a repeat of the procedure or to clear the area for a different job. To fill in the

NORMAL WORKING AREAS



Physical Data For An Average Man

Weight	155 lb.
Height	5'-8"
Length of arm	30.8"
Humerus	12.9"
Radius	10.6"
Hand	7.3"
End joint of 2nd finger	1.0"
Estimated inches from shoulder pivot point to table edge	3.5"



THE NEW YORK HOSPITAL

WORK SIMPLIFICATION

PROPOSAL FOR IMPROVEMENT

No. ___
Rec'd ___

Submitted by: _____ Date _____

Department: _____ Phone Ext. _____

DESCRIBE YOUR PROPOSAL:

ORIGINATOR: Fill out completely. Forward this proposal form with your Flow Charts or other material to Room M-117 inspected, and then returned to you for consideration by your Supervisor.

REVIEW OF PROPOSAL BY SUPERVISORS

Date Reviewed	Comments and Approvals with signatures of Supervisors

ESTIMATED YEARLY SAVINGS	Distance in Feet	Time in Minutes
Present Method		
Proposed Method		
Difference		
Times occurrence per day		
Times occurrence per year (300 days)		
Estimated yearly savings in feet & minutes		
Estimated yearly savings in miles and hours (divide by 5280 ft. & 60 min.)		
Other Savings		

ESTIMATED COST OF INSTALLATION

Installation Cost _____

Equipment Cost _____

ORIGINATOR'S SIGNATURE

(Space Below for Methods)

Date	Progress of Proposal	Pending
		Approved Not Installed
		Installed
		Rejected

do operations therefore is to accentuate them and to assist in the later questioning of the details. For every transportation and delay recorded in the details, the distance in feet, time and quantities of items involved should be actually measured and recorded in the appropriate column of the flow process chart.

In the preparation of the flow process chart it may be well to supplement this data with a flow diagram giving the layout of the area over which is indicated by a line, the flow of the item being followed on the process chart.

Summarize

After recording all data concerning the job, we summarize all facts and enter them in the block in the upper left hand corner of the form.

We find that our completed chart now contains all the data obtained by carefully watching a particular job, and upon examination we may realize that we have observed things which have never been brought to our attention before. The job has been separated from its background and surroundings. The make-ready, the do and the put-away phases of the operation have been accentuated. All the information of the job has been condensed so that we can easily visualize the process in its entirety. The mere act of making the chart helps to automatically develop a better method.

Question The Steps

Kipling said, "I keep six honest serving men, they taught me all I know, their names are What and Why and Where and When and Who and How." Now that we have a charted picture of the job as it is actually being done, we set about to analyze it, and in questioning each detail of the method we put Kipling's six men to work. In challenging each detail on our chart we ask: What is the purpose of this step?, Why is it necessary?, Where should it be done?, When should it be done?, Who should do it?, and How should it be done? We ask if the operation can be eliminated, combined or subdivided. Can it be done during the idle period of another operation? Is the sequence the best possible? What could we gain by changing the sequence? Should the operation be done in another department to save handling costs.

In the analysis of the present method it is well to have assistance from people working directly

in the operation, for the individual who knows most about the job is the one who actually does it. By asking his assistance we enlist his cooperation in the development of the new method which serves as a valuable foundation for future training. In this analysis a positive attitude must be taken that a new method can be developed. We must abhor the phrase, "Well, we've always done it that way." An industrial executive once remarked that if he found that an operation had been done the same way in his plant for six months, he felt that it should be seriously questioned; and if he found that it had been done the same way for a year, then he knew very well it should be improved.

Develop New Method

In developing a new method then, we should concentrate on the make-ready and the put-away portions of the job. We should look at transportations and storages for the possibility of re-grouping of equipment and the combining of items to eliminate travel or reduce the number of trips. We should attempt to reduce handling, lifting, carrying or trucking of items if possible. We should eliminate handling work done by skilled operators. The pharmacist should be utilized to the fullest extent possible in his professional capability. All mechanical means possible should be used to keep materials moving in one direction. Proper loading, unloading, and stacking should be used. If two operations cannot be combined, perhaps a transportation could be combined with an operation, or an inspection with an operation. If combining operations is difficult, then perhaps we can change their sequence, and it is at this point that we find the flow diagram useful. If we cannot change sequence then we should attempt to breakdown and simplify the operation. By this approach then, with the facts we have obtained, we develop a new and better method.

With a new method developed possibly requiring new equipment or changing interdepartmental routines it is necessary to enlist the cooperation of the hospital administration as well as of people outside the Pharmacy and of departments which service the Pharmacy or are serviced by the Pharmacy.

To sell and coordinate the new method, we describe, summarize and compare the new method with the old on a Proposal For Improvement form. A copy of this form, as illustrated, is self explanatory. It can be modified to meet the needs of individual problems. We can see that it contains the major considerations necessary to an effective presentation of a new method for adoption on an interdepartmental level. Where a new method involves only intradepartmental routine the proposal form, while not essential to the initiation of the new method, is certainly useful in pointing up savings and advantages accruing to the efficiency and personnel of your department and in promoting greater job satisfaction.

Through the flow process chart, the flow diagram, and the proposal form, labor saving devices and equipment such as tablet and capsule counting machines, label printing machines, pressure filter devices, and vacuum bottle filters may be completely justified to your administration.

Applications to Hospital Pharmacy

In the application of work simplification to hospital pharmacy we not only develop a more efficient pharmaceutical service but we find that we have also developed a keener interest in, as well as a better understanding of people. The importance of your membership on the patient care team will be clarified as you sit down with individuals from other departments, perhaps for the first time, to work on a job simplification problem together. In working with other departmental personnel on such problems as deliveries of drugs and other materials, the processing and scheduling of requisitions, the development of an improved narcotic control system, you will find new interests in your own responsibilities as a hospital pharmacist. You will realize that although these other people have not told you so, they have not really forgotten you as you may have begun to suspect.

The work simplification approach to routine problems will help you to avoid an obsolescent attitude which comes as the result of habitual thinking based upon fixed routines.

New Approaches

If it were not for fresh approaches to problems in hospital pharmacy, this very SOCIETY, in session here today, might never have been born. The experience gained by exposing yourself to new methods and by solving new problems, will broaden your outlook, and make the attack on subsequent problems easier. And finally, work simplification will help you to understand and practice a basic positive philosophy of progress which will be reflected in your attitude toward the operations of your department. This positive attitude and the personal factors of contagious action which result are considered the most important part of leadership capacity.

Our individual and collective activity in work simplification can affect our future as professional individuals as well as the future of hospital pharmacy itself.

CURRENT STATUS OF DISPOSABLE NEEDLES AND SYRINGES

by MILTON W. SKOLAUT *and* WILLIAM H. BRINER

FOR THE PAST SEVERAL YEARS, the Pharmacy Department of the Clinical Center has been actively attempting to stimulate interest by the medical supplies industry in various disposable items. A significant number of these articles have been developed due to a concerted effort on the part of many hospitals and others who use these devices in order to maintain an efficiently and economically operating unit, without compromising on the quality of patient care.

As a result of the constant increase in salaries of hospital personnel, which in many cases are still too modest, the cost of preparing sterile items in a central sterile supply service has risen to a new high. A factor which contributes greatly to this constantly increasing cost index is the lack of utilization of automatic processing equipment for reasons of space limitations, large initial investment, and a rather high unit cost of items processed in this manner due to the relatively small number of items required by any given institution.

Another problem in this respect has been a lack of uniformity in packaging, differences in most frequently used sizes, and other variations between hospitals. It is only through constant cooperation between several hospitals and the industry at large, in addition to a trend toward standardization in the several areas that comprise the total hospital operation, that the great progress in the development of many disposable medical supply items has been possible.

Although this presentation will be limited almost entirely to needles and syringes, certain considerations may be applied equally well to all disposable items.

MILTON W. SKOLAUT is Chief and WILLIAM H. BRINER a staff member of the Pharmaceutical Development Service of the Pharmacy Department, Clinical Center, National Institutes of Health, United States Public Health Service, Department of Health, Education and Welfare, Bethesda 14, Maryland.

Cost Studies Unreliable

Many cost studies reported in the literature are not valid when studied objectively, for, when more than a casual perusal is made of the statistical analyses and, indeed, even the fundamental precepts on which the research is based, inconsistencies and inaccuracies become apparent. Surveys show the cost of preparing a needle and a syringe for patient care usage to be somewhere in the range of $0.0473 to $0.20. This varies with each institution according to the number of syringes and needles processed per unit time, the salaries of the individuals involved in these procedures, and the type and extent of use of the processing equipment available. There are, therefore, no generalities which can be offered with respect to the cost of processing these items and, when a survey is made, the results can be applied with any degree of accuracy only to the institution participating in the survey.

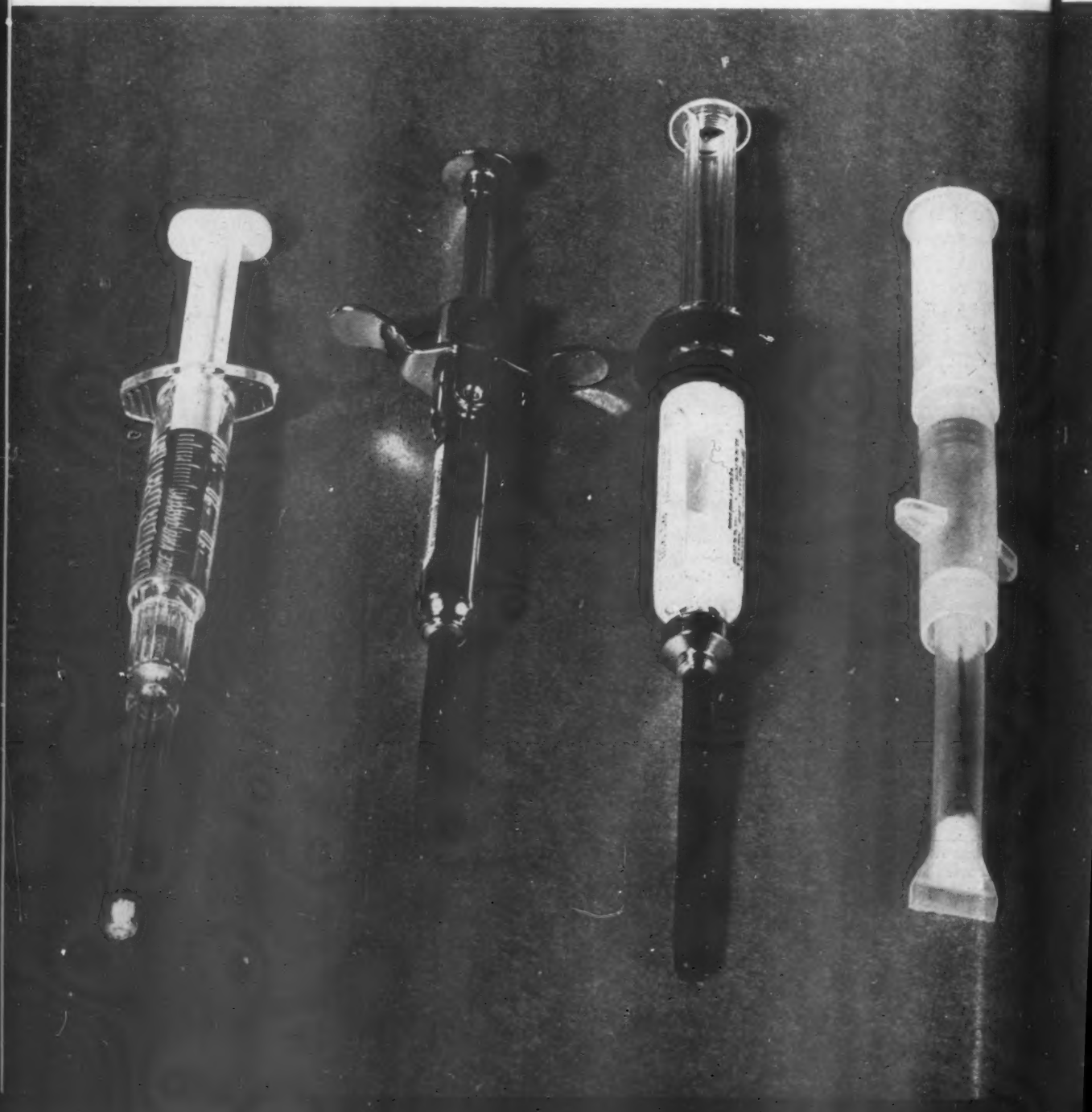
In addition, the personnel performing the tasks under consideration are usually aware that the survey is taking place. This may, in many cases, introduce a statistical error into the results on the part of both the employee and the observer. In a situation such as this, human nature itself would be sufficient to cause the employee to work at a more rapid rate with a higher degree of efficiency than is customary. On the other hand, the observers in these studies all too frequently are individuals completely divorced from the hospital field, and as a consequence, have little knowledge and even less understanding of the procedures being evaluated. As a result of this, both conscious and unconscious bias may appear in the evaluation. For these reasons, it would seem that a more accurate approach to this kind of cost analysis would be possible if the survey were devised and conducted by individuals thoroughly familiar with hospital procedures and,

perhaps even more important, to make the observations required in the study without the knowledge of the participating personnel. Admittedly, this type of analysis would be difficult to effect, but the results of research conducted in this manner could most assuredly be started with a far greater degree of validity than is usually possible.

Intangible Costs

In addition, there exist many intangibles, of which the direct cost accounting into a dollars and cents value is difficult, if not impossible. These exist in the several areas of the hospital involved in the processing and use of these materials, such as pharmacy, central sterile supply, purchasing, medical staff, and nursing staff. For example, the evaluation of the work load in central sterile supply will aid immeasurably in determining whether certain disposable items may advantageously be procured to provide time for the implementation of additional services not previously available from this facility, services which cannot be cost-accounted directly into the overall patient care expenses. In addition, a consideration fundamental to an evaluation such as this is the determination of whether or not the use of certain disposable items will minimize the time required to handle these items throughout the hospital

Examples of disposable units

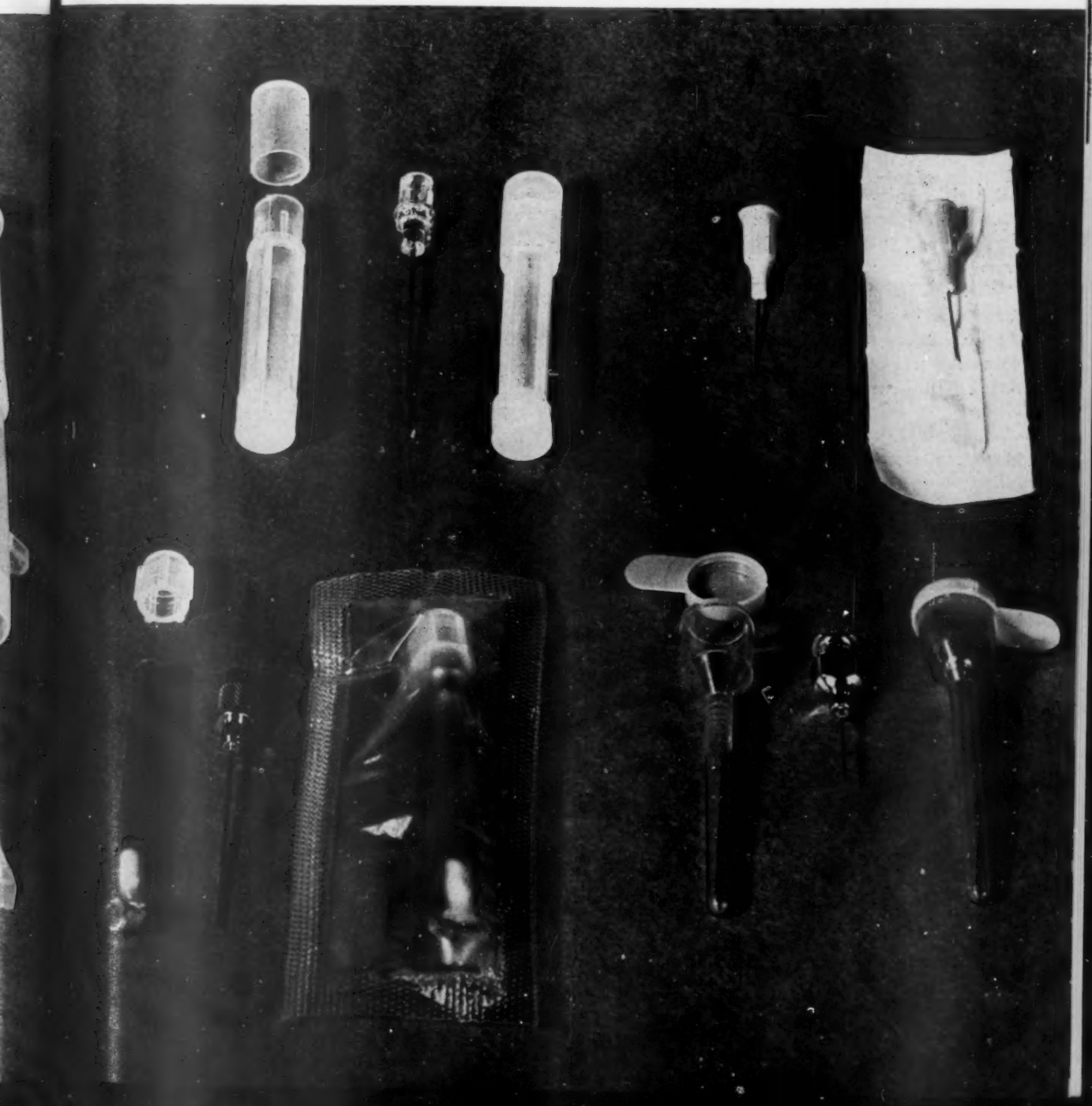


areas concerned. These include the pharmacy for drugs, the central sterile supply, purchasing, receiving, and stores. A very important aspect of this determination is the fact that a decreased handling time on the part of the medical and nursing staffs will allow an increased amount of time available for additional patient care activities by these individuals.

Advantages

In the case of needles and syringes, the ever present danger of transmission of infection and the production of a pyrogenic response in a patient can be greatly minimized by the use of disposable items. The complete absence of, or at best, the somewhat haphazard sterility testing procedures employed by certain institutions only serve to emphasize the importance of this point. Certain prepackaged medications supplied in a single dose unit containing a disposable needle and syringe, in addition to avoiding a possible break in sterility, such as frequently results from a withdrawal from a multiple-dose vial, also provide for a greater accuracy of dosage and a decrease in waste of the medicament. These single dose disposable units may also reduce materially the incidence of serum sickness and anaphylactoid sensitivities in hospital personnel, for scarifying or puncture of the skin of these persons occurs most frequently when the needle is withdrawn from a multiple-dose

Illustrations of different types of needles along with sterile containers



vial prior to administration of the drug. Obviously, the use of disposable needles, in particular, will accomplish much toward avoiding the occurrence of infectious hepatitis and homologous serum jaundice in central sterile supply and blood bank personnel.

Certain costs involved in the examples cited may be calculated very accurately, but in the majority of cases, reliable assessments are not possible. In the latter cases, the problems involved must be studied by responsible administrative persons and resolved in a manner to best meet the needs of the particular institution.

The hospital pharmacist, as a result of the scope of his knowledge and his participation in the total hospital activity in both clinical and administrative functions, should be a very interested and a valuable member of the survey group.

Disposable Items Increasing

One thing is certain: the acceptance and usage of disposable items in hospitals is increasing each year. Inherent in this increased usage is a decrease in production and marketing costs of these materials. An even greater rate of change in both the usage of these items and the number of items available will be evidenced within the next several years.

There follows a somewhat limited tabulation of disposable items currently available with which the authors are familiar. Inclusion in this listing does not necessarily imply a personal recommendation by the authors or an endorsement by the United States Government, nor does the exclusion of any products currently available indicate a lack of acceptability of these products. The tabulation is not intended to be comprehensive, but is included only to cite examples of types of disposable items commercially available at the present time.

Disposable Needles, Non-Sterile

Supplier: Roehr Products Company, Inc.
Cost: $37.25 per 1000 needles
Remarks: Available with aluminum hubs and stainless steel cannulae; may be reused, but manufacturer strongly recommends discarding after single use; provides a new, sharp needle, free from infectious material remaining from prior usage; needles must be suitably packed and sterilized by the institution, but the loss due to pilferage, breakage, and resurfacing is eliminated.

Disposable Needles, Sterile

Supplier: Sterilon Corporation
Cost: Range from $0.0675 for a 25 gauge ⅝" needle to $0.09 for an 18 gauge 1½" needle.
Remarks: Needles are sterile, ready for use; may be reused, if desirable, after reprocessing by the institution.

Needle and Syringe, Sterile

Supplier: Wilburn Corporation
Cost: $0.137 for a 2 ml. syringe and needle
Remarks: Needle cannula molded into tip of syringe, not removable; syringe fabricated from polyethylene, used as any conventional syringe is used; completely disposable.

Supplier: Becton Dickinson and Company
Cost: Approximately $0.14 to $0.15 for a 2 ml. syringe and needle.
Remarks: Glass barrel syringe with rubber gasketed plunger; needle permanently attached; used as any conventional syringe.

Needle, Syringe and Medication, Sterile Single Dose Unit

Suppliers: Pfizer Laboratories, under trade mark of "Steraject;" and Wyeth Laboratories, under trademark of "Tubex."

Cost: Range of $0.20 to $0.30 per unit.

Remarks: Only most popular medications now available, such as antibiotics and narcotics, the latter only in certain areas of the country; includes a sterile disposable needle and syringe purchased by the pharmacy, thus eliminating all central sterile supply service and many distribution costs; of great advantage to private institutions is the fact that cost of needle, syringe, and medication is readily determined and may be charged directly to the patient; generally, receive excellent acceptance by professional personnel and patients.

Conclusion

The rising costs of processing and use of syringes, needles, and other materials in hospitals are noted. Certain inconsistencies and inadequacies of surveys and those who conduct them in hospitals are elucidated, and recommendations for improvement in survey methods are suggested. The advantages inherent in the use of disposable items are compared with certain disadvantages in the utilization of the more conventional reusable materials. A limited presentation of types and costs of disposable units commercially available is given with certain descriptive information included. Many additional disposable items are currently under investigation and clinical trial, and it is expected that more will be marketed within the near future in view of their wide acceptance and utilization. The ideal needle and syringe, which still remains to be produced and stands as a challenge to the ingenuity of American industry, would be so fabricated and packaged as to offer a sterile unit ready for use without further processing, at a reasonable cost to the user, and of a composition which would make impossible the reuse of the unit. That this challenge will be met and conquered by American industry is certain.

Internship Objectives

FOR HOSPITAL PHARMACY

by ROBERT CALVO

Four basic objectives are offered which should underlay a carefully planned hospital pharmacy internship. The author illustrates a few activities which serve to provide experience in professional aspects of dispensing, professional relations, pharmacy administration and, finally, culminating in an intern-preceptor relationship which will contribute to the prestige and progress of hospital pharmacy.

A HOSPITAL PHARMACY INTERNSHIP is of little value if it is concerned only with preparing a candidate for state registration or licensure. The internship program should be planned to provide formal educational activities and conditions should be designed to give the intern a rich background of personal experience. The ultimate goal of such an internship program should be to introduce the candidate to all types and phases of hospital pharmacy.

ROBERT CALVO has recently completed an internship in hospital pharmacy at Hackensack Hospital, Hackensack, New Jersey.

Objectives

The following objectives should serve as a nucleus for a successful hospital pharmacy internship program:

1. To provide, to the fullest extent possible, familiarization with the handling and dispensing of prescriptions and drugs in order to develop a background which will thoroughly prepare the intern for state registration, and introduce him to

A view of the dispensing area, Hackensack Hospital

the practice of pharmacy in accordance with the highest standards and attainments of the profession.

2. To provide experience and training in professional relations with the public and allied health professions.

3. To prepare the intern to assume full responsibility for the supervision, organization, and maintenance of a hospital pharmacy in the most desirable manner and in the light of advanced thinking and current progress. It is therefore essential that the intern be given experience in every phase of the department's administration and supervision. Obviously, his skill in each phase of activity will be commensurate with his personal knowledge and interest, his length of experience, and the quality of his preceptor's guidance.

4. To foster an intern-preceptor relationship which will be beneficial to each and will contribute to the elevation of professional standards.

Dispensing

Expertness in the handling and dispensing of drugs is naturally a product of many years of experience preceeded by a thorough formal, academic background. It would be empty pride indeed to say that one year's internship could compensate for this experience. Nevertheless, a well coordinated internship program can strive to offer a reasonably rich presentation of drug and prescription experience in accordance with the local demands of the area. To satisfy the first objective stated previously, the intern should take part in the handling and dispensing of drugs and all types of prescriptions encountered in the hospital pharmacy. Any unusual compounding problems or items should be called to the attention of the intern so he may take an active part in the solution of such problems. A standard system of checks and balances within the pharmacy serves to impress the intern with the necessity for adequate controls of all medication leaving the department and emphasizes care in its preparation.

Teaching

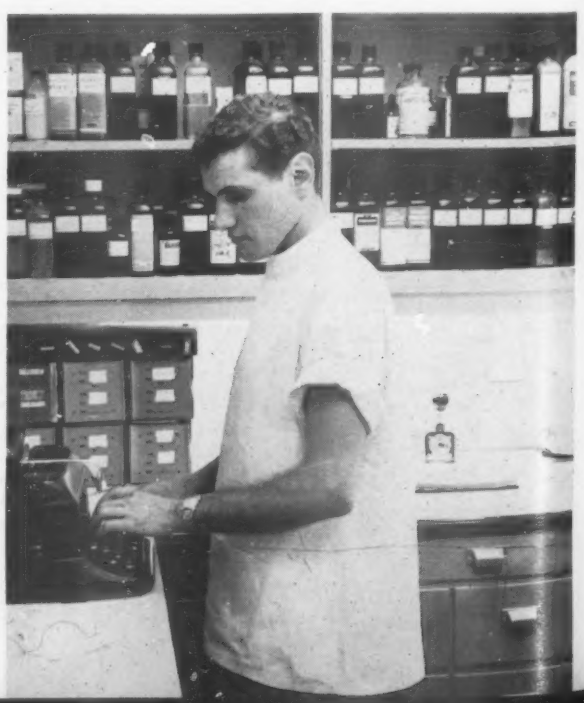
An excellent opportunity is afforded the intern when the hospital is affiliated with a nursing school. Arrangements should be made allowing the intern to prepare and deliver various lectures in pharmacology to student nurses. The author has gratifyingly witnessed a program in which the Pharmacy Department presents the first year pharmacology course and lecture seminars to each of the upper classes. The latter seminars are of two kinds. One is concerned with newer drugs and pharmacological concepts popularized since the nursing student's first year course, and the second type is an in-service program. The in-service seminar consists of several lectures devoted to drugs used and associated with a single department of the hospital *i.e.,* Obstetrics-Gynecology etc. The best way to learn is to teach. This is a philosophy that has proven itself over the years. In hospitals not affiliated with nursing schools the feasibility of delivering lectures on new drugs to graduate nurses of a "refresher" nature should be considered. Such opportunities provide the impetus for keeping the pharmacy intern well informed on the newer drugs and developments in his field.

Literature

The intern should be required to read all product literature coming into the pharmacy and be encouraged to read all professional publications. The preceptor and staff should stimulate intra-departmental discussion of professional articles and new products. The relative merit of all new products should be reviewed in light of newer concepts and possible inclusion in the hospital formulary. Assigning the intern the responsibility of setting up and maintaining product literature files and a "new product section" provides him with experience in methods designed to keep the pharmacist well informed on new products and reports of drug evaluations.

Lectures

Many educational opportunities pertinent to hospital pharmacy avail themselves during the course of each year. The intern should enroll in such classes as a part of his internship requirements. The author has gained much from attend-



Robert Calvo, author of accompanying article

Weighing counter showing ultra violet light

ing a Pharmacy Institute of the American Hospital Association, a course in small volume parenterals, and miscellaneous seminars and lectures offered by the local colleges. Professional groups offer many educational lectures at group meetings *i.e.*, the hospital pharmacy program at the A.A.A.S. and the A.Ph.A conventions, local chapter meetings of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the American Pharmaceutical Association etc. University and other professional contacts are especially valuable during the internship period because the intern is in a position to correlate many academic impressions into his practice of hospital pharmacy.

An excellent opportunity is afforded the entire department by virtue of the intern's transitory position between college and practice. He should discuss various operational procedures of the pharmacy with members of his college faculty. By such contact he will become exposed to opinion and suggestion which will enable him to maintain a broad perspective and clear outlook on the different phases of hospital pharmacy operations. It is a common practice for one to "get use to" a familiar system and thus lose the objective outlook which is essential to increasing efficiency and guaranteeing continued improvement. Suggestions for improving pharmacy operations are necessary for the entire department's progress. Attendance at meetings of professional pharmaceutical organizations is itself an educational component and thus should be defined as an obligation in the internship program.

Only a few activities illustrating the technical and professional expressions of the practice of pharmacy which must be a planned part of the internship program have been offered. The first objective proposed by the author is flexible enough to be applied to all departmental conditions *i.e.*, product stability studies or other activities designed to encourage individual research.

Professional Relations

To the intern the second proposed objective, "experience and training in professional relations . . . " cannot be taken lightly for it is the core of professional success. In hospital pharmacy it means more than being nice to people. Activities must be delegated to the pharmacy intern which will increase his understanding of the problems of other interrelated health professions and of the general public. Understanding is the qualifying factor which will enable the intern to cooperate with other groups under conditions of mutual respect. More specifically, it is the understanding of the other's problems and attitudes that lends for harmony and cooperation.

A breakdown of public relations into its meaningful components would usually start with the general public. The intern must be prepared to meet and talk with the general public in his professional capacity for a significant portion of his future lifespan. The intern meets the general public each time he fills an outpatient prescription, each time he explains a refill procedure to a patient and during a great many other characteristic

contacts associated with dispensing. The intern must be able to understand the public's desires and attitudes where the practice of pharmacy is involved, regardless of the public's ability or desire to obtain medicine. He should be encouraged to discuss openly pricing policies or any other questions of a professional nature that confront him. Professional displays during National Pharmacy Week and National Hospital Week should be an assigned obligation of the pharmacy intern. Such displays serve to educate the public and to place pharmacy in its proper perspective.

Professional Relationships

The success of the hospital formulary system is an illustration of how important good pharmacy-physician relations are to the operation of a hospital pharmacy department. The intern should attend each meeting of the Pharmacy and Therapeutics Committee. He should attend some of the medical staff meetings solely for the purpose of acquiring a broader perspective on all the major problems physicians encounter. A great deal of understanding and respect can be stimulated by these associations. Attendance at Pharmacy-Nursing Liaison Committee meetings will give the intern an insight into administrative problems which exist between the pharmacy department and nursing service. During his internship, the author set up and delivered a three-hour orientation program to each new group of graduate nurses coming into the hospital. By explaining the various procedures and services the department offers, the nurses are better prepared to utilize these services more rapidly and more efficiently. Also, in the same hospital, all student nurses are required to spend two full days in the Pharmacy under the supervision of the pharmacy intern so that all operational procedures may be explained in detail and many may be demonstrated. A great deal of understanding can be obtained from contacts such as these and, if properly applied, they will contribute constructively to nursing-pharmacy relations. In hospitals where the foregoing programs and comparable committees do not exist, the pharmacy department should take an active part in initiating them.

Interdepartmental Relationships

Good interdepartmental relations are also included in the objectives for a pharmacy internship for they are conducive to the over-all efficiency of the pharmacy department. Aside from the educational value derived by the interns visiting other departments, a recognizable contribution to professional relations is achieved and both respect and understanding between the pharmacy and these interrelated departments are advanced many fold.

Intraprofessional relations are forwarded by the intern's active membership in professional organizations. Special internship committees should be organized to encourage organizational activity and participation by interns in the constructive work of professional pharmaceutical groups.

The groups mentioned above play a vital part in the hospital pharmacist's work, thus it is only fair that the pharmacy intern be encouraged to play an active part in building public and professional relations and to become conscious of all major problems in the sphere of the health professions.

Management Functions

To fulfill the last objective the intern must receive experience in every phase of the department's activity. He should engage in maintaining inventory controls, purchasing, setting up various departmenal records, establishing pricing policies, relocation of stock and space reapportionment, manufacturing operations, formulary revisions, and all other phases of departmental activities. In such a short time as an internship period, no individual can become expert in all phases of such operations, but the internship program should be designed to give the intern the opportunity to be introduced to the over-all picture and to understand all the parts that make up the whole. The activities of each hospital pharmacy differs in scope so that it seems unwise to have the intern spend too much time in any single phase of operation, except dispensing. Rather, emphasis should be placed upon factors necessary to the department's success and efficiency. It should be the intern's responsibility to visit other hospitals and to familiarize himself with their general plan of operation.

The atmosphere in each hospital pharmacy should be one which stimulates good intradepartmental relations. Only under such conditions can the fourth objective for pharmacy internships be accomplished easily. Fostering a good intern-preceptor relationship that will benefit both individuals is a vital part of the present internship system in pharmacy. The intern must not simply sit back and draw from his preceptor's rich background of experience. He should, rather, contribute his knowledge of recent educational and scientific advances to the practicing pharmacist. Together they may profit from their valuable relationship and be better prepared to advance the standards of professional pharmacy.

Aerial view of Philadelphia General Hospital

work and schedule assignments in the pharmacy of the PHILADELPHIA GENERAL HOSPITAL

by B. J. WEXLAR

IT WILL BE AGREED, I believe, that all hospital pharmacies cannot operate under a similar plan. This is particularly true of city hospitals. An exchange of information as to what other hospital pharmacists are doing affords one the opportunity of adapting these methods to one's own particular needs.

The adoption of any given procedure involves many considerations such as the physical set-up, equipment, number of employees in the department, number of floors, and the number of patients to be served. Will a procedure meet with the approval of the visiting, resident, intern, and nursing staffs? Of major importance is the acceptability of the procedure by the administrative staff.

While it is reasonable to assume that, as pharmacists, we have the knowledge to select the proper procedures, one often hears of opposition from members of the various hospital staffs. Be it the medical or administrative staff, it is well to bear in mind that they, like ourselves, wish to contribute their best efforts.

Basically, it is our own department that we are concerned about. It must be remembered, however, that the administrative staff is concerned about many departments. Various department heads may be suggesting changes or asking for changes. Hence, before presenting any request for equipment, increase in personnel or changes in procedures, all facts should be weighed carefully. It is also to be remembered that while there may be agreement with the request, monies may not be available.

Hospital

The Philadelphia General Hospital covers an area of approximately five blocks. It consists of a central corridor approximately 900 feet long with

B. J. WEXLAR is Chief Pharmacist at the Philadelphia General Hospital, Philadelphia, Pa.

Above: Chief Pharmacist B. J. Wexlar at his desk. Left: Pharmacist weighing ingredients for bulk compounding.

24 wings, each wing five stories high. The newest wing is eight stories high. The bed capacity is 1,783. The staff includes 120 residents, 107 interns, 100 graduate nurses, and 400 student nurses. The hospital contains 59 nursing stations.

Selection of Drugs

Unlike those in private institutions, the pharmacy in a city hospital is not a profit-making department. We are ever conscious of our duty to make the latest drug developments available to our patients. Since our hospital is also a teaching institution with a large number of residents and interns, we appreciate the teaching value of a modern therapeutic armamentarium. In order to exercise control over the selection of drugs we have a Pharmacy and Therapeutics Committee which evaluates all drugs. A drug which has not been approved by the Pharmacy and Therapeutics Committee and is required in the treatment of a patient may be obtained on an emergency form signed by the physician and approved by the medical director.

Our drug requirements are obtained through bids. These are prepared by the Chief Pharmacist and his assistants and sent out by the Procurement Department twice a year. This means that we must anticipate our requirements six months ahead. This is quite a challenge since we attempt to keep within a budget and not have too much or too little of any one item. To accomplish this, we keep a close watch on the turnover of all items. Completed requisitions are submitted to the medical director and the administrator for approval.

We maintain a perpetual inventory, hence we know our exact inventory at all times and the turnover of any one item. These records, as well as the posting of cost, source of supply and date purchased, are kept up-to-date by our office force.

The Pharmacy fills approximately 760 prescriptions daily, 595 for inpatients and 160 for outpatients, along with an average of 40 drug baskets. Each drug basket contains up to 50 items. Many days we must send out two trucks at one time.

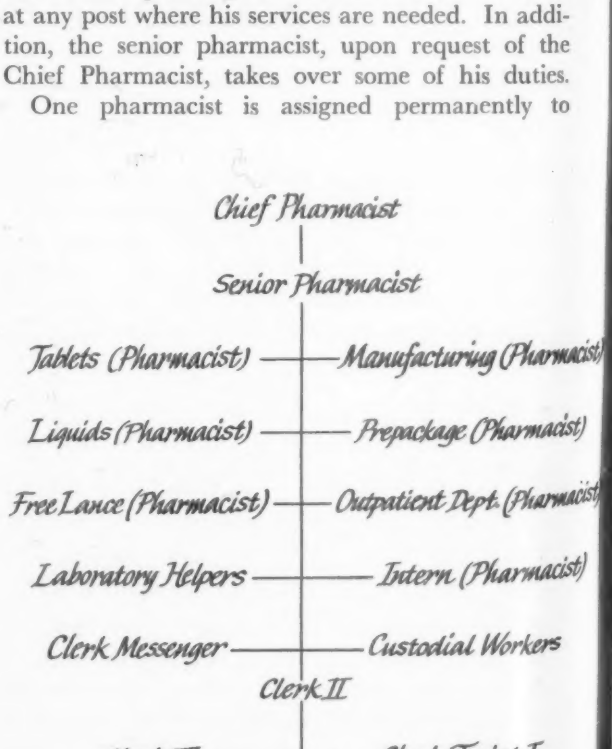
Pharmacy Staff

In addition to the Chief Pharmacist, our staff is composed of seven pharmacists, one pharmacy intern, two laboratory helpers, two custodial workers, and one clerk-messenger. The clerical section of the Pharmacy Department is staffed by two clerks (II) and a clerk-typist (I). One of the clerks supervises the office personnel.

The Pharmacy Department must be organized to service all departments properly and yet be flexible enough to cope with situations and special requests that arise from time to time.

The senior pharmacist, in consultation with the Chief Pharmacist, has charge of the pharmacy personnel. This pharmacist assigns duties, assists in inventory control, and in preparing requisitions. The senior pharmacist is also available to assist at any post where his services are needed. In addition, the senior pharmacist, upon request of the Chief Pharmacist, takes over some of his duties.

One pharmacist is assigned permanently to



View of Pharmacy, Philadelphia General Hospital

manufacturing and has the assistance of a laboratory helper. As the Pharmacy is open Saturdays, each pharmacist, including the manufacturing pharmacist, takes his turn working on Saturdays with a day off during the week. The pharmacists work a total of 40 hours a week. The Pharmacy is open until 8:00 P.M. The pharmacists, with the exception of the manufacturing pharmacist, take their turns working Wednesday evenings, but come to work at 11:00 A.M. instead of 8:30 A.M. on that day. When necessary, the manufacturing pharmacist helps in the Outpatient Department during lunch periods.

One pharmacist is assigned to each of the following schedules: tablets, liquids, Outpatient Department, and prepackaging. One pharmacist, besides the senior pharmacist, is unassigned so that he may assist at any post.

These assignments are on a rotating basis. They change every two days, except the outpatient assignment which changes daily. The object of the rotating assignments is to permit the staff to become acquainted with the entire department and to remove the possibility of monotony. Although each pharmacist is assigned to a particular schedule, each must help with other work when he is not busy and when his services are needed on other work schedules.

Coupled with the above, each pharmacist is assigned to a specific drug stock section. Each is responsible for checking items received for his section and entering these items on stock control cards. About once a week he issues drugs to open stock and deducts these items from the stock control cards. He must fill out an issue form and turn it into the Pharmacy office. The sections are divided as follows: ampuls, antibiotics, biologicals, chemicals, pharmaceuticals, tablets, and bottles.

Duties

Some of the duties of Pharmacist II are as follows: performs professional and minor management work in the compounding and dispensing of drugs and other pharmaceutical supplies; plans and assigns work of subordinate professional and nonprofessional pharmacy employees to meet the pharmaceutical requirements of a large hospital; assists in the requisitioning of pharmaceuticals and informs subordinates of changes in procedures, formulas, and pricing of prescriptions; and performs related work as required.

Some of the duties of Pharmacist I are as follows: performs professional work in the compounding and dispensing of drugs and other pharmaceutical supplies; manufactures ointments, solutions, syrups, suppositories, elixirs, and other pharmaceutical preparations in large quantities; keeps a worksheet showing items manufactured, quantities made, and ingredients used; prepackages tablets, capsules, powders, and ointments; and performs related work as required.

Office, Pharmacy Department, Philadelphia General Hospital

The pharmacy intern, in addition to the educational program, rotates from schedule to schedule.

Nonprofessional Personnel

In addition to assisting where required, one of the custodial workers takes shipment of drugs from the storehouse to the Pharmacy, helps the pharmacist place the drugs in the stock room, keeps stock clean and in order, and delivers drug baskets when required. He also keeps a stock control card on prescription bottles, puts labels on bottles before they are prepackaged, helps to keep the place clean, and performs related work as required.

Another custodial worker delivers the drug baskets and picks up requisitions and empty bottles. When necessary, he helps the pharmacist prepackage a few liquids, keeps the floor and department clean, and performs related work as required. Drug baskets are delivered twice daily, at 10:00 A.M. and 1:00 P.M. Requisitions picked up on the 1:00 P.M. delivery are delivered at 10:00 A.M. on the following day. Those picked up on the 10:00 A.M. delivery are delivered at 1:00 P.M. on the same day.

The clerk-messenger prepackages tablets for the Outpatient Department, helps the pharmacist with the dispensing of insulin during the clinic hours, and performs related work as required.

Another laboratory helper assists the manufacturing pharmacist. He also helps the pharmacist prepackage tablets for inpatients, and performs related work as required.

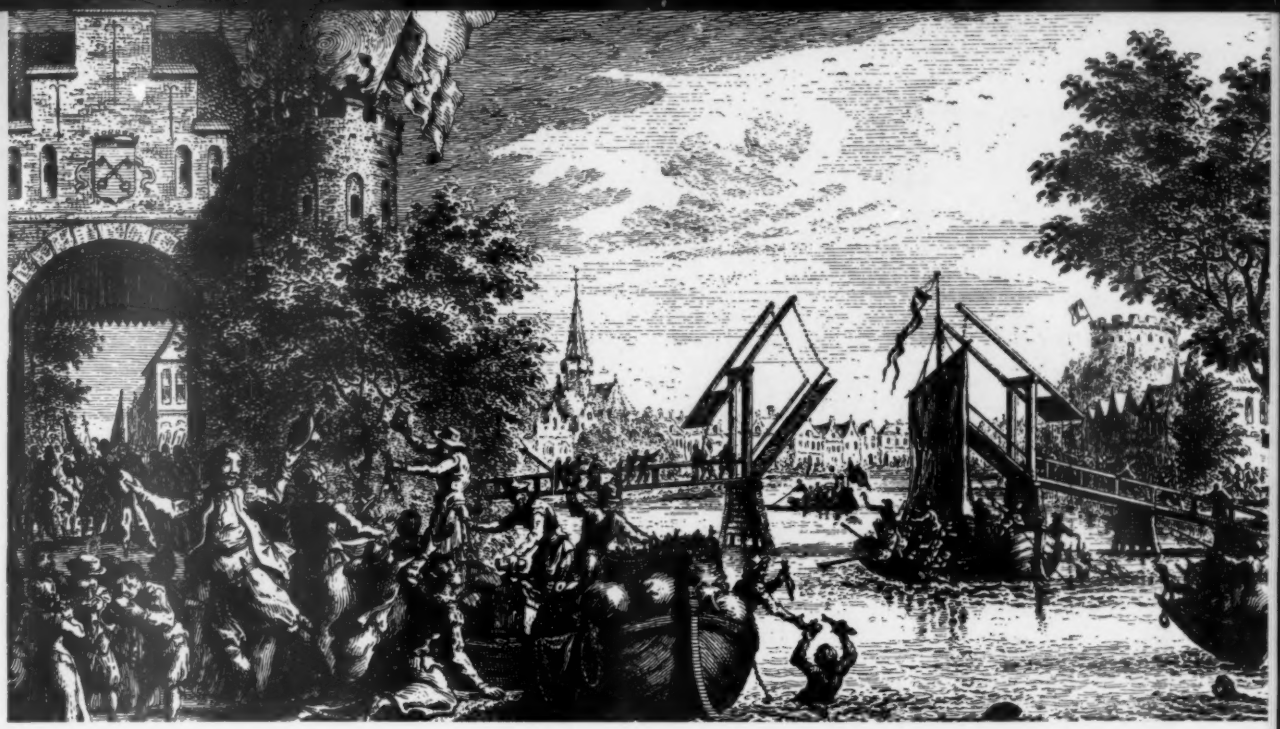
Duties of Clerk-Typist I include the following: types work schedules, letters, inventory cards, requisitions, receiving reports for payments, stencils, physical inventory sheets, etc.; relieves Clerk II when necessary; takes money received from the previous day, with receipts, to the registrar's office daily; takes time schedule to personnel office on Mondays; answers telephones; and performs related duties.

The duties of Clerk II may be summarized in the following manner: keeps record book of daily issues received from pharmacists for items taken from reserve stock; keeps record book of requisitions received daily from the wards; keeps record of daily insulin prescriptions; keeps record book of cash received in the Pharmacy daily for prescriptions dispensed; keeps monthly ledger of total amount of inpatient and outpatient prescriptions dispensed in the hospital; is responsible for posting all drug shipments and issues in inventory ledger in order to maintain a running inventory; performs any related clerical duties necessary, as instructed by her supervisor.

The Clerk II-Supervisor has the following responsibilities. She supervises the office, consisting of two clerks (one Clerk II and Clerk-Typist I); assists the Chief Pharmacist with the requisitioning of drug supplies; enters shipment of drugs in merchandise receipt book; prepares "merchandise receipts" for typist to type, "receiving reports and requisitions for payment," "processes receiving reports and requisitions for payment," recording information on them; makes comparisons with purchase orders and prepares them for the Chief Pharmacist's signature (in his absence she signs them for the Chief Pharmacist); supervises the running of the Perpetual Inventory Ledgers; balances the ledgers, checks for errors, makes comparative check with Physical Inventory Reports and stock control cards maintained by pharmacists; does the pricing of the drug requisitions and tabulates their total costs; does the pricing and tabulation of physical inventory reports; runs Monroe Calculator; prepares employees' time sheets; answers the telephone for the Chief Pharmacist; and does any related work as requested by the Chief Pharmacist.

Chief Pharmacist

The activities of the Chief Pharmacist come under many headings which I will mention only briefly. They are as follows: he is in charge of all Pharmacy personnel; formulates administrative procedures; recommends policies regarding interdepartmental relationships; prepares recommendations to administration for pharmacy development; prepares reports and supervises purchases; is responsible for narcotic and alcohol inventories and reports; checks merchandise received; spot checks drugs at nursing stations; assists in editing the formulary; is Secretary of the Pharmacy and Therapeutics Committee; interviews medical service representatives and disseminates product information to the staff; and performs related work as required.



Old engraving illustrating the siege of Leiden, 1574, which led to the founding of the University there

The 17th Congress of Pharmaceutical Sciences of the F. I. P.

by JACK COOPER

THE HISTORY OF THE FAMOUS UNIVERSITY city of Leiden is lost in antiquity, but the existence of Roman ruins indicates that it must have been an attractive economic or military location long before the native inhabitants had discovered their recipe for the alcoholic extract of juniper berries known as gin. Less than a century after Columbus started the stream of emigration to America, Leiden was a pleasant fortified city with canals and an impressive system of dikes to keep the cellars dry. The existence of these dikes proved to be even more valuable when the Spaniards beseiged the city in 1574. When the courageous defendents lost their customary portly appearance, the dikes were cut and ships were able to bring provisions to the inhabitants of the flooded town.

As a curious reward for the heroic defense of the city, William of Orange in 1575 founded the University of Leiden. The surprised citizens accepted the gift graciously and after the necessary drying period, set to work to make their new educational edifice worthy of its location. Within half a century of its founding, the presence on the campus of such scholars as the historian Joseph Scaliger, the jurist Hugo Grotius and the progressive theologian Jacobus Arminius, raised Leiden University to an eminent position in the ranks of

JACK COOPER is Director of the Pharmacy Research and Development Division of Ciba Pharmaceutical Products, Inc., Summit, N. J.

Leiden Town Hall and Carillon Tower

European universities. In spite of increasing competition from other schools with superior extramural sports programs, the faculties of law and medicine are even today recognized as outstanding.

Although less well-known in international circles, the faculty of pharmacy has also made many contributions in its field. The broad outlook of Dutch pharmacy is characterized by the contributions made not only in scientific matters but in support of the professional organizations of pharmacy. The selection of Leiden University as the meeting place for the first interim Congress of Pharmaceutical Sciences of the Fédération Internationale Pharmaceutique was, therefore, a well deserved tribute to our pharmaceutical colleagues of The Netherlands.

Organized by the Scientific Section of the F.I.P., this was actually the 17th Congress of Pharmaceutical Sciences sponsored by the Federation with sessions held on September 12, 13 and 14, 1957 in various rooms of the university. The Congress attracted over 225 members from 20 different countries including such distant ones as Japan, Lebanon, Israel, Turkey, and the United States.

Heparin Symposium

Following addresses of welcome by Professor P. A. H. de Boer, Rector of the University, Sir Hugh Linstead, President of the F.I.P. and Professor R. Ruyssen, President of the Scientific Section of the F.I.P., a special symposium on "Some Aspects of Heparin" occupied the remainder of the first day. Dr. F. L. J. Jordan, Faculty of Medicine, University of Utrecht, described the current status of heparin from the clinical point of view with special emphasis on differences between this drug and dicoumarol in the treatment of thrombo-embolic diseases. The speaker also indicated that heparin, in addition to its effects on the blood clotting process, also influences blood lipids and possesses antiserotonin activity. The next speaker, Dr. D. S. Robinson of Oxford University, elaborated on the effects of heparin on the fat transport system. The mechanism of this heparin clearing reaction was explained as due to the hydrolysis of the triglyceride of the lipid particles to a free fatty acid with the formation of a soluble fatty-acid-albumin complex. At the present time, it is not certain whether the clearing action appears normally in the blood or whether it is due to an extravascular enzyme system whose appearance in the blood artificially follows the injection of heparin.

The paper by P. Blonde, Laboratories Fournier Freres, Paris, demonstrated the difficulties in the physico-chemical control of heparin. From beef lung, the common starting material for the ex-

traction of commercial heparin, it has been possible to isolate heparins of different composition and activity. This subject was further reviewed by A. Winterstein of Basle who emphasized the difficulties in setting up standards for therapeutic heparin. In his opinion measurement of inhibition of fibrin coagulation is probably the most accurate technique. Commercial samples, tested by this method, were generally satisfactory.

In view of the importance of the anticoagulants in therapeutics, the symposium on heparin was enthusiastically received as representative of the problems confronting scientists engaged in pharmaceutical research. On the second and third days of the Congress, it was necessary to present papers simultaneously in several sections. About 45 subjects in analytical chemistry, organic synthesis, microbiology, pharmacology, and physical pharmacy were discussed following the presentation of formal papers by authors from many different countries.

Structure and Bactericidal Activity

Although the quality of the presentation was uniformly high, space permits only a brief summary of those which are of the greatest interest to hospital pharmacists. Dr. H. Vogt of the Pharmaceutical Institute, University of Kiel, discussed the relationship between chemical constitution and bactericidal activity. It is his view that antibacterial substances vary in the manner in which they act on bacterial cells but the presence of both hydrophilic and lipophilic groups in the molecule of the substance is a definite advantage since penetration into lipoid and aqueous phases of tissue fluids is required. Water solubility of phenols was obtained by preparing water-soluble salts of phenolphosphoric acid and of 8-oxyquinolines by conversion into quaternary ammonium compounds. The di-p-n-butyl-phosphoric acid ester and N-methyl-5-thiocyanogen-8-butoxyquinoline methylsulfate were particularly active antibacterial agents.

Halogenated Oxyquinolines

Dr. N. Diding of the Apotekens Kontrollaboratorium in Stockholm found iodochlorhydroxyquinoline, di-iodohydroxyquinoline, and dichlorohydroxyquinoldine active on gram-positive organisms but only slightly effective on gram-negative organisms. The addition of small amounts of Tween 80 enhanced the activity of these halogenated oxyquinolines including their effect on the gram-negative type.

The University, Leiden, Holland

Inactivation of Antibiotics

In an interesting study dealing with the inactivation of antibiotics by vitamins, Dr. J. Dony-Crotteux of the Service de Controle des Medicaments A.P.B., Brussels, demonstrated the inactivating effect of vitamin B complex on antibiotics. More specifically, the author showed riboflavin inactivates tetracycline by acting as a sensitizer which precipitates a photo-oxidation of the antibiotic.

Bacteriostatics for Parenterals

Dr. C. L. Sargent of the Ministry of Health, London, summarized a report of the Bacteriostatic Sub-Committee of the Conference on the Control of Antibiotics dealing with bacteriostatics for parenteral injections of procaine penicillin. Experimental studies have demonstrated that the stabilizing effect of sodium citrate diminishes with increasing concentration of penicillin. Customary concentrations of phenylmercuric nitrate, p-hydroxybenzoates, and benzyl alcohol were not satisfactory bacteriostats for procaine penicillin because of poor bactericidal activity in the presence of the medicament or incompatibility with the medicament or vehicle. Although cetrimide in a 0.01 percent concentration was satisfactory, samples of the substance from different sources varied in bactericidal potency.

Effect of Copper on Stability

Professor S. S. Schou of the Royal Danish School of Pharmacy continued to show his strong interest in the field of stability of drugs by presenting a paper on the detrimental effect of copper on the stability of pharmaceutical preparations. Using epinephrine and nor-epinephrine solutions, it was found necessary to keep the copper limit below 0.02 parts per million in order to ensure stability. This limit is a requirement even in the presence of the protective sulfite ion.

Assay of Parenterals

Of positive interest to hospital pharmacists interested in assuring the quality of their parenteral preparations was a paper by R. Hofstra of Brocades, Stheeman and Pharmacia Limited in Meppel discussing the control of injections by means of ultraviolet absorption spectrophotometry. This pharmacy has found the colorimetric technique to be of great value in determining the purity of the drugs used, the effect of the sterilization process on the preparation, and the stability of the injection during shelf life.

Tablets

Although eccentric (single punch) tablet compressing machines are seldom used today in the United States except for teaching purposes, the paper by Professor K. Munzel and P. L. Seth of Hoffmann-LaRoche and Co. Ltd., Basle, partly explained the reasons. The authors found that the "apparent density" of compressed tablets is jointly influenced by the magnitude of the pressure, the length of time, and the manner of application of the pressure. A relatively smaller pressure can achieve the same "apparent density" of compressed tablets if applied from both sides and if allowed to act for a longer period. The relative strength of the upper and lower surfaces of compressed tablets is less uniform when compressed from only one side. A bilateral compression results in a more uniform strength of the different tablet surfaces.

Isotonicity and pH

In an interesting, statistically sound, evaluation of the sensitivity of the human eye to hypo- and hypertonic solutions, Dr. C. Trolle-Lassen of the Laboratory of Danmarks Apotekerforening, Copenhagen, found that the human eye does not react to instillation of solutions with freezing point depressions between 0.41° and 0.77°C. corresponding to sodium chloride solutions between 0.7 and 1.4 percent. The author also found that solutions with a *p*H range between 7.3 to 9.7 have no disagreeable effect when instilled into the human eye whereas *p*H values under 5.8 and over 11.4 nearly always cause irritation.

Meeting in Brussels

It is anticipated that the next Congress of Pharmaceutical Sciences will attract an even larger number of excellent papers since a record number of pharmaceutical scientists will undoubtedly attend. The sessions will again form part of the program of the F.I.P. which next year will meet in Brussels during the week of September 8th. In addition to the manifold activities sponsored by the Federation, the presence of the World's Fair in Brussels will act as an additional magnet. In addition to the regular sections of hospital pharmacists, control directors, secretaries of pharmacopoeias, editors of pharmaceutical publications, etc., the first meetings of the new section on industrial pharmacy will also take place. Among the millions of visitors to Brussels in September 1958, there will be pharmacists from every country of the world meeting in pleasant conclave to advance knowledge in the field of the pharmaceutical sciences.

Statement of the Special Committee of the ASHP

on the

Formulary System and Alleged Substitution

This is a statement of the Special Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS appointed to explore problems of mutual interest with a Special Committee of the National Pharmaceutical Council.

The purpose of this statement is to clarify the basis of the formulary system and to refute the charge of alleged substitution which is said to take place in hospitals operating under this system.

Definition of Substitution

Substitution is defined by the National Pharmaceutical Council as follows:

"Substitution is the dispensing of a different drug or brand of drug in the place of the drug or brand of drug ordered or prescribed without the express permission of the prescribing physician."

Thus, it follows from this definition that substitution takes place if:

1. A different drug or brand of drug is dispensed.
2. Without the express permission of the prescribing physician.

In other words, two conditions have to be present in order for substitution to take place.

Definition of Pharmacy and Therapeutics Committee

The Pharmacy and Therapeutics Committee, composed of physicians and the chief pharmacist, is a committee of the medical staff which represents the official, organizational line of communication and liaison between the medical staff and the Pharmacy Department. This Committee assists in the formulation of broad professional policies regarding the evaluation, selection, procurement, distribution, use, safety procedures, and other matters relating to drugs in hospitals. Specifically, the purpose of the Committee is (1) to develop a formulary of accepted drugs for use in the hospital, (2) to serve as an advisory group to the hospital pharmacist on matters pertaining to the choice of drugs to be stocked, (3) to evaluate clinical data concerning drugs requested for use in the hospital, (4) to add to and to delete from the list of drugs accepted for use in the hospital, (5) to prevent unnecessary duplication in the stock of the same basic drug and its preparations, and (6) to make recommendations concerning drugs to be stocked on the nursing units and other services.

This Committee is one aspect of medical staff self-government. It is responsible to the medical staff as a whole and recommendations made by the Committee are subject to medical staff approval.

Definition of Formulary System

The formulary system may be defined as follows:

The formulary system is a method used by medical staffs of hospitals, working through a Pharmacy and Therapeutics Committee composed of physicians and the chief pharmacist, to evaluate and to select from among the numerous medicinal agents available those that are considered most useful therapeutically, together with the dosage forms in which they may be administered most effectively.

Thus, under the formulary system, the Pharmacy and Therapeutics Committee performs the same function for the medical staff of the hospital as the Committee on Scope does for the Committee of Revision of the Pharmacopeia of the United States.

Conclusion

From an examination of the foregoing it may be seen that:

1. The Chief Pharmacist in his role as Secretary of the Pharmacy and Therapeutics Committee has a formal, organizational relationship with the medical staff which does not exist in other areas of pharmacy practice.
2. The policies involved in accepting and dispensing drugs are under the control of the medical staff.
3. A policy to accept and dispense drugs under their generic names is approved by the medical staff.
4. This policy is similar to that used by the Pharmacopeia of the United States and the National Formulary, as far as the acceptance of drugs is concerned.
5. All members of the medical staff are informed of the policy.
6. No deception is involved.
7. By approval of a policy to accept and dispense drugs under generic names, the medical staff gives their express approval to this method, and
8. Under such conditions substitution is not involved in the operation of the formulary system.

therapeutic TRENDS

edited by WILLIAM JOHNSON

Tessalon—An Antitussive Agent

The antitussive activity of Tessalon is evaluated and the results are presented by Shane *et al* in *Can. Med. Assoc. J. 77*:600 (Sept. 15) 1957. Of interest is the method by which the antitussive activity of this drug is determined. Twenty patients, carefully screened for absence of any spontaneous cough, were selected for this study. Each patient received aerosol inhalations of 15 percent citric acid solution as a cough-producing agent because of the proven uniform and consistent response of the test subjects to the same threshold of the stimulating agent. The efficacy of Tessalon in doses of 100 mg. was compared with that of codeine in doses of ½ grain. It was found that codeine, in the dose named, decreased the frequency of induced cough to 50 percent of the pre-medication figure, while Tessalon, in 100 mg. doses, decreased the frequency of induced cough to 20 percent of its pre-medication figure. This would indicate that, in the doses stated, Tessalon is approximately two and one-half times as effective in cough suppression as codeine. No undesirable side-effects resulted from the administration of this drug. The Tessalon for this study was supplied by the Ciba Company of Canada.

Ethoheptazine—An Analgesic Agent

Ethoheptazine (1-methyl-4-carbethoxy-4-phenyl hexamethyl-enimine) is an analog of meperidine. As a result of a study of seven-membered ring analogs of meperidine in 1954, ethoheptazine seemed to offer the most promise for continued investigation. The effectiveness and safety of ethoheptazine have been studied in 330 patients requiring analgesia for a wide variety of medical and surgical conditions. Two additional groups of patients, totaling 127, were given ethoheptazine with aspirin. Satisfactory analgesia regardless of etiology of painful state was achieved in 73 percent of ambulatory patients. Sixty-two percent of hospitalized patients responded, but required a higher dosage. Postpartum pain was satisfactorily controlled in 82 percent of the patients treated with ethoheptazine alone and in every instance when treated with combined ethoheptazine with aspirin. The occurrence of insignificant untoward reactions was noted in 4 percent of both ambulatory and hospitalized patients. The combination of ethoheptazine with aspirin enhances the likelihood of achieving satisfactory analgesia. This study is reported by Batterman *et al* in *Am. J. Med. Sci. 234*:413 (October) 1957. Ethoheptazine for this study was supplied by Wyeth Laboratories.

Glycyrrhetinic Acid—Anti-Inflammatory Properties

Glycyrrhetinic acid, the active principle in licorice, used topically, has valuable anti-inflammatory properties resembling those of hydrocortisone, but obviously not identical. The potentialities of this anti-inflammatory agent have not been fully explored, and many possible indications remain undiscovered. In an effort to determine its value, a series of dermatologic trials have been carried out using "biosone G.A." ointments which, according to the manufacturers, contain the active isomers of glycyrrhetinic acid. A table is used to summarize results. This study is reported by Colin-Jones in *Pract. 1067*:600 (May) 1957.—from an abstract in *Am. Pract. Dig. Treat. 8*:1605 (October) 1956.

Bone Marrow—Intravenous Infusion In Patients Receiving Radiation and Chemotherapy

Since cases of radiation disaster may occur, and since bone-marrow deficiency from radiation or chemotherapy does occur in the normal course of clinical medicine, an effort has been made to determine the availability and usefulness of bone-marrow infusion for the treatment of these conditions in man. Observations from a year's experience in collecting, storing, and using bone

marrow are recounted by Thomas *et al* in *New Eng. J. Med. 257*:491 (Sept. 12) 1957. The effects, in a small series of patients, of intravenous infusion of cellular suspensions of marrow are reviewed. Marrow may be obtained from fetal and adult cadavers and from biopsy and surgical specimens, preserved in glycerol at -80° C. and administered, intravenously, to patients with safety. The indications, contraindications and general potential field of usefulness of marrow transplantations are discussed.

Penicillinase—Treatment of Penicillin Reactions

Minno and Davis describe the treatment of penicillin reactions with penicillinase in *J. Am. Med. Assoc. 165*:222 (Sept. 21) 1957. Treatment included the use of penicillinase alone and also in combination with antihistamines. The use of penicillinase in the treatment of hypersensitivity reactions to penicillin is based on the logical knowledge that circulating penicillinase reduces demonstrable penicillin blood levels to zero for prolonged periods of time, thus rendering the penicillin nonallergenic. When used in 32 cases of moderate to severe hypersensitivity reactions to penicillin, the results of treatment with penicillinase were definately encouraging and apparently superior to measures previously in standard use. Two principal types of reactions were observed, namely, urticaria with generalized pruritus and serum sickness reaction. No anaphylactic reactions were seen. Penicillinase is a product of Schenley Laboratories.

Dipipanone Hydrochloride—An Analgesic

Dipipanone is DL-6-piperidino-4:4-diphenylheptan-3-one. The results of the administration of this analgesic are presented by Gillhespy *et al* in *Brit. Med. J.11*:1094 (Nov. 10) 1956. All cases treated suffered from pain severe enough to justify the use of a potent analgesic. Adequate pain relief was obtained in the great majority of cases of post-operative pain following major gynecological surgery and of pain due to a variety of acute and chronic medical conditions. Only 3 out of 200 cases treated failed to obtain any relief from this drug. The optimal dose was found to be 20 mg. in the medical cases and 25 mg. in the postoperative cases. The onset of analgesia after subcutaneous injection occurred within 10 minutes and maximal relief was obtained in about 20 minutes in most cases. The effect lasted for approximately five to six hours. There was no obvious depression of respiration or tendency to drowsiness, nor was there any local reaction or pain at the site of injection. Side effects (nausea, vomiting, sweating, and giddiness) were rare, their incidence in relation to the number of doses administered being 4 to 5 percent.

G-25671 Metabolite—A Uricosuric Agent

In the course of study of the antirheumatic and uricosuric properties of a series of phenylbutazone analogues, it was found that G-25671, a thio analogue of phenylbutazone, possesses marked uricosuric properties. It is metabolized rapidly and virtually completely in man. The result of present work by Burns *et al* which appears in *J. Pharmocol and Exp. Therap.* 119:418 (March) 1957 describes the isolation from the urine of a metabolite of G-25671, that has been identified as the sulfoxide. The sulfoxide, when administered to gouty subjects either in single intravenous doses or in repeated daily doses, produced striking uricosuria. Its uricosuric effect is considerably more pronounced than that of G-25671 and it may in fact account for the major part of the effect of the parent drug on uric acid excretion. Experience thus far suggests that the sulfoxide has weak antirheumatic activity. The finding that the sulfoxide is a more potent uricosuric agent than G-25671 suggests its clinical trial in the treatment of gout. No toxic reactions have been observed with its use in 17 gouty patients, but the period of observation is much too short for any statement concerning toxicity.

MC-9367—A Carbonic Anhydrase Inhibitor

MC-9367, which has been developed at the Squibb Institute for Medical Research, is a propanyl derivative of acetazolamide. Its therapeutic properties are similar to those of acetazolamide. In this study by Balistocky and Gettes as reported in *Am. J. Ophth.* 43:730 (May) 1957, MC-9367 was used to lower intraocular pressure. The drug in a single dose administered orally is an effective agent in lowering the intraocular pressure in humans. The greatest period of effectivity is two to four hours after administration and the greatest degree of lowering intraocular pressure occurred in the eyes of patients with glaucoma. No paresthesias and no toxic effects were noted after single dosages. In no instance was MC-9367 effective where acetazolamide had also failed.

timely drugs

Adenovirus Vaccine

. . . for prophylaxis against common respiratory and conjunctival infections caused by adenovirus serotypes 3, 4 and 7, is now available from Parke, Davis and Co. It is an aqueous, trivalent vaccine preparation of inactivated and adenoviruses, combining the three types in approximately equal proportions. For prophylaxis against infection produced by adenoviruses, types 3, 4 and 7, a single injection of 1 ml. administered intramuscularly or subcutaneously is recommended. A separate heat-sterilized syringe and needle should be used for each patient in an effort to prevent transmission of homologous serum hepatitis and other infectious agents. The vaccine is available in 5 ml. vials.

Adrestat

. . . a systemic hemostat designed to aid in the prevention and control of bleeding, has recently been announced by Organon, Inc. An oxidation product of epinephrine, Adrestat (adrenochrome semicarbazone, Organon) is recommended for use by the intramuscular route as a systemic hemostat in idiopathic purpura, familial hereditary telangiectasis, epistaxis, pulmonary bleeding, and bleeding from other sites. It is also useful in controlling bleeding without correcting underlying pathologies in hematuria, metrorrhagia, and menorrhagia. It is particularly useful in the prevention and treatment of bleeding during and after surgery involving a broad vascular base, such as operations on the nasopharynx, prostate or bladder. Orally, capsules and lozenges of the drug are recommended for use as maintenance therapy in these indications after active bleeding has been controlled by intramuscular injection. The dosage in mild low-grade bleeding is 5 mg. administered intramuscularly every three or four hours until bleeding is brought under control. In the preparation of the patient for nasopharyngeal surgery, three capsules or lozenges should be administered for five days before the operation. The lozenges are particularly useful post-surgically. Adrestat (F) is supplied in packages of five 1 ml. ampuls, each ampul containing 5 mg. adrenochrome semicarbazone, available as 130 mg. of carbazochrome salicylate. Each Adrestat capsule contains 2.5 mg. of the active drug, 5 mg. sodium menadiol diphosphate, 50 mg. purified hesperidin, and 100 mg. ascorbic acid, and is available in boxes of 30. The lozenges contain 2.5 mg. of the drug and other ingredients as in the capsules, and are supplied in boxes of 20 lozenges.

Cervilaxin

. . . a highly purified brand of relaxin, has been released by the National Drug Co. It is a hormone extracted from pregnant sows' ovaries by a special process which assures uniformity of strength and quality. The drug shortens labor and facilitates delivery. In the recommended dosage, the action of Cervilaxin is concentrated in the cervix and surrounding tissue. It causes softening of the cervix to facilitate dilatation. Obstetricians have used oxytocin with Cervilaxin to obtain maximum correlation between uterine contractions and cervical dilation. There is also clinical evidence that Cervilaxin alone facilitates delivery. Best results have been reported with the combined administration with oxytocin. Oxytocin is first administered, adding 0.1 ml. of the U.S.P. injection to 250 ml. 5 percent dextrose or normal saline. Cervilaxin is then administered, adding 40 mg. to 250 ml. 5 percent dextrose or normal saline, after cervical dilatation to 2 to 3 cm. and cervical effacement by at least 75 percent have been established. The drug is available in 2 ml. vials containing 20 mg. Cervilaxin per ml., in boxes of 1 and 6 vials.

Diagnex Blue

. . . a carbacrylic cation-exchange resin diagnostic test, has been announced by E. R. Squibb and Sons. The resin is in reversible combination with azure A dye, and in the presence of free gastric acid, the blue dye of the resin is exchanged for hydrogen ions of the acid. The dye that is thus split off is absorbed and promptly excreted in the urine, usually imparting to the urine a characteristic blue or blue-green color. If no free acid is present in the stomach, the dye remains attached to the resin and does not appear in the urine within the prescribed test period. When the dye appears in the urine after the test period, it is of no diagnostic significance. When the test provides presumptive evidence of hypochlorhydria or achlorhydria, further studies of the patient's gastic acid status are indicated. The determination of gastric acid secretion has been reported as a valuable step in the diagnosis of cancer of the stomach, pernicious anemia, and gastric polyps. The patient is given the Diagnex Blue unit containing (1) dye-resin granules, (2) caffeine sodium benzoate tablets for the stimulation of acid secretion, and (3) labels for urine samples. He is

requested to comply with simple but explicit instructions in the package. Diagnex Blue is available in 2 Gm. packets containing approximately 100 mg. of azure A dye. With each packet of dye-resin are included two tablets containing 0.25 Gm. caffeine sodium benzoate. The drug is supplied in units of 5 and 50 tests, each with an assembled, ready to use color comparator.

Vesprin

. . . a new agent for better management of psychotic patients, has been announced by E. R. Squibb and Sons. It is useful in schizophrenia, manic states, and psychoses associated with organic brain disease. Because the phenothiazine structure has been modified, Vesprin (trifluprom azine, Squibb) shows an enhanced potency with far less sedative effect. The recommended initial adult dosage is 25 mg. administered three times daily. This dose may be increased until the desired clinical effect has been achieved, or until unwanted side effects become a problem. The initial dose for children is 10 mg. three times a day. The suggested starting dose in geriatric patients is 10 mg. given three times daily. Vesprin is supplied in tablets of 10 mg., 25 mg., and 50 mg. in bottles of 50 and 500.

Dornavac

. . . pancreatic dornase for inhalation therapy, has been released by Merck Sharp & Dohme. It is a stabilized preparation of the enzyme, desoxyribonuclease, derived from beef pancreas. Aerosol therapy with the drug is indicated for the specific purpose of reducing the tenacity of pulmonary secretions in disorders characterized by mucopurulent exudation in the tracheobronchial tree. It rapidly attacks and degrades desoxyribonucleoprotein—the substance composing 30 to 70 percent of purulent bronchial discharge. Since Dornavac acts on extracellular accumulations and disintegrating cells, and not on living tissue, its potent lytic effect is restricted to debridement of surface accumulations of purulent and viscous material. The suggested dosage is 50,000 to 100,000 units, administered in an ordinary atomizer or by aerosolization with any suitable device for pressure breathing, one to three times daily for a period of two to six days, until improvement occurs and the maximal response is obtained. It is supplied in a vial with vacuum tight closure, each vial containing 100,000 units of pancreatic desoxyribonuclease, together with a 2 ml. vial of sterile diluent.

Furestrol

. . . suppositories for urethritis have been marketed by Eaton Laboratories. These are suppositories for the specific treatment of senile urethritis—a common cause of dyspareunia, dysuria and other pelvic complaints in menopausal and postmenopausal women. Each suppository contains Furacin (nitrofurantoin, Eaton) 0.2 percent, diethylstilbestrol 0.0077 percent (0.1 mg. per suppository) and diperodon hydrochloride 2 percent, in a water-dispersible base. Furestrol provides estrogen to correct the atrophic tissue changes of senile or involutional urethritis. Furacin is a highly effective antibacterial against associated urethral infection, while diperodon, a rapidly-acting local anesthetic, promptly relieves pain and burning. One suppository is inserted into the urethra, morning and night. The patient should remain supine for 10 minutes after insertion, to permit melting and spreading. Treatment should continue for at least one week and until symptoms disappear. This usually requires two weeks. The suppositories are hermetically sealed in boxes of 12.

Medrol

. . . an anti-inflammatory steroid, is now available from the Upjohn Co. Due to a methyl substitution, Medrol (methylprednisolone, Upjohn) achieves a split between the anti-inflammatory and mineralocorticoid activities of the delta-steroids, prednisone and prednisolone. It has a wide range of effectiveness in rheumatic diseases, allergic diseases, generalized dermatoses with an allergic component, acute ocular inflammatory disease involving the posterior segment, and in various diseases responsive to anti-inflammatory corticosteroids such as adrenogenital syndrome, nephrosis, ulcerative colitis and for temporary remission in leukemia. The recommended Medrol dosages are suggested as average total daily doses and are intended as guides only. In general, daily doses can be estimated to be about ⅔ those of prednisolone. As with other oral corticosteroids, the total daily dose should be given in four divided doses, preferably after meals and with a snack at bedtime. Medrol is available as 4 mg. scored tablets in bottles of 30.

Pro Actase

. . . a direct potent physiologic enzyme for the debridement of wounds, is now marketed by Ortho Pharmaceutical Corp. Pro Actase Profibrinolysin (plasminogen) is the basis of the fibrin-lysing system, the normal component of human blood necessary for wound healing. It is activated by streptokinase to form the active enzyme, fibrinolysin (plasmin). Activated, it dissolves fibrinous exudates in wounds and adjacent tissues, aids in removal of necrotic tissue, debris and exudate, improves drainage, decreases infection, and consequently promotes healing. Clinical results have been obtained in the debridement and healing of infected wounds, chronic leg ulcers, abscesses, chronic surgical wounds, and sinus tracts. In treatment with Pro Actase, it is desirable to add another enzyme, hyaluronidase. This enzyme acts on the hyaluronic acid of the intercellular substance, liquefying it, and permitting the diffusion of nutrient substances and oxygen as well as antibiotics into the wound. The activated Pro Actase and hyaluronidase solution may be applied in the form of a wet compress and covered with a petrolatum gauze dressing. The compress should be in contact with the wound for 24 hours. The combined solution may be instilled directly into deeper wounds or sinus tracts. The drug is available in a combination package containing one ampul with 10,000 Fibrinolytic units of Pro Actase Profibrinolysin and one ampul of 150 U.S.P. units Diffusion (hyaluronidase, Ortho).

selected pharmaceutical abstracts

and summaries of other articles interesting to hospital pharmacists

edited by LEO F. GODLEY *and* CLIFTON J. LATIOLAIS

INTESTINAL BACTERIAL ADSORBENTS

Adsorption Studies on Clays II. The Adsorption of Bacteria by Activated Attapulgite, Halloysite, and Kaolin, Barr, Martin: J. Am. Pharm. Assoc., Sci. Ed., 46:490 (Aug.) 1957.

Bacterial adsorption by activated attapulgite, halloysite, and kaolin clays was studied on suspensions of *Staphylococcus aureus, Proteus vulgaris, Salmonella enteoides,* and *Shigella paradysenteriae* at pH 6.8. Activated attapulgite adsorbed nearly twice as many *Staphylococcus aureus* and four times as many as halloysite. There was low adsorption of the latter three bacteria. A method for the study of the bacterial adsorption has been developed. The fact that a change in the bacteria-clay ratio did not result in a significant increase of bacteria adsorbed and further, that the four bacteria and clays are negatively charged, suggested that the reduction of bacterial count might be a mechanical sedimentation of the bacteria in suspension by the clays rather than adsorption.

NORMAN HO

STABILITY OF SODIUM PARA-AMINOSALICYLATE

The Stability of Sodium Para-Aminosalicylate in Aqueous Solution, Kokoski, C. J., Dissertation Abstracts, 17:1958 (Jan.) 1957.

Sodium para-aminosalicylate in aqueous solutions undergoes rapid meta-aminophenol formation and darkening. Sealing the solution with carbon dioxide under pressure increased the rate of decarboxylation instead of reversing the reaction. Sodium bisulfite and sodium formaldehyde sulfoxylate prevented the darkening, but accelerated the rate of reaction. Buffering the solution to a more alkaline pH using potassium acid phosphate—sodium hydroxide or sodium borate resulted in a higher rate of decarboxylation and darkening and the addition of antioxidants failed to reduce the decomposition. Replacing air with nitrogen gas over the solution inhibited the darkening effect and not the decarboxylation.

On the other hand, Versene Na_4, sodium sulfite, Versene Na_4 with sodium sulfite, and n-isopropylethylenediamine reduced the darkening and decarboxylation. Versene Na_4 (0.05%) with sodium sulfite (0.1%) reduced the rate of decarboxylation by approximately 75 percent.

Investigation of meta-aminophenol in aqueous solution found the solution to darken and form a black precipitate. Sodium bisulfite and sodium sulfite prevented the darkening.

NORMAN HO

IODOPHORS AS DISINFECTANTS

Iodophors as Disinfectants, Lawrence, C. A., Carpenter, C. M., and Naylor-Foote, A. W. C., J. Am. Pharm. Assoc., Sci. Ed. 46:500 (Aug.) 1957.

Iodophors are compounds of elemental iodine complexed with nonionic wetting agents acting as solubilizers. Their bactericidal effectiveness, uses, and superior advantages over iodine, that is (1) the enhanced bactericidal activity of iodine, (2) the minimal odor and staining tendencies, and (3) the practically nontoxic and irritating properties, are reviewed in the literature search.

The investigation was conducted to compare (1) the fungicidal and bactericidal activities of several disinfectants in distilled water, hard water, and serum, (2) the germicidal activity of an iodophor on tubercle bacilli, and (3) the sporicidal activity of the iodophor on *Bacillus subtilis* spores. The disinfectants included Wescodyne (iodophor), Roccal (benzalkonium chloride), Amphyl (mixture of phenolic compounds), and phenol. The bacteriological procedure is described.

From the experimental evidence, the following conclusions were postulated:

1. The bactericidal and fungicidal activity of the disinfectants was in the following order: Wescodyne, Amphyl, Roccal, and phenol. While Wescodyne was closely correlated in activity to Amphyl, it was far superior to Roccal.
2. The presence of hard water had no adverse effects on the disinfectants except for Roccal.
3. With the exception of phenol, all the disinfectants had a depreciable drop in activity in the presence of horse serum.
4. No evidence of tuberculosis was found in experimental animals receiving a suspension of tubercle bacilli treated with 1:320 Wescodyne.
5. Wescodyne destroyed the spores of *Bacillus subtilis* up to a 1:21 dilution within a 24 hour exposure period.

NORMAN HO

WEIGHT VARIATION OF COMPRESSED TABLETS

Studies on Tablets III. Weight Variation of Compressed Tablets, Hasegawa, J., Pharmaceut. Bull. (Japan) 5:15 (Feb.) 1957.

Four factors thought to affect the deviation of weight of compressed tablets were studied. These were (1) tablet base, (2) punch diameter, (3) size of sieve used in granulation, and (4) speed of compression.

Experimentally, tablets were compressed over short periods as the above four factors were varied. Three tablet bases were used. One contained precipitated calcium carbonate, lactose, and starch, another was of lactose only and the third was composed of lactomin and starch. Punches of 7, 10 and 13 mm. were used. Sieve sizes varied from 14 through 19 mesh. Tablet machine speeds of 42 and 76 tablets per minute were tested. After compression the deviations in tablet weight were statistically analyzed. Results showed that changes in tablet base did not significantly alter tablet weight variation. Punch diameter and size of sieve used in granulation proved highly significant. Decreasing either the punch diameter or size of sieve increased the variation in tablet weight. Variance in tablet machine speed did not significantly change deviations in tablet weight.

In his article the author includes a table of recommended punch diameters and sieve sizes devised to keep tablets within U.S.P. limits of tablet weight variation.

JOHN LUCASSE

PROCAINE IN GLUCOSE INJECTION

Equilibrium of Procaine -N - Glucoside Formation in Parenteral Solutions --Containing Procaine and Glucose, Ikeda, K., Pharmaceut. Bull. (Japan) 5:101 (Apr.) 1957.

Primary aromatic amines are known to combine with glucose and form aryl - N - glucosides in aqueous solution. In parenteral solutions containing procaine and glucose this reaction produces a noticeable reduction in anesthetic activity and is therefore undesirable.

The reaction was shown to be an exothermic one with the amount of procaine-N-glucoside existing at the equilibrium point dependent upon the temperature of the solution. Experimentally, samples of 0.5% procaine and 5% glucose were brought to equilibrium at various temperatures and

there procaine-N-glucoside content determined. Results showed that at 20°C., 66.5%, and at 100°C., 26% of procaine was in the combined form. From these figures it can be concluded that a 5% glucose solution stored at 20°C. will require 1.44% procaine in order to maintain 0.5% free procaine. Also, because of the exothermic nature of the reaction, storage of procaine-glucose solutions in a refrigerator is not recommended.

JOHN LUCASSE

INACTIVATION OF ANTIBIOTICS BY VITAMINS

The Inactivation of Antibiotics by Vitamins, Dony-Crotteux, J., J. de Pharm. de Belgium 39:179 (May-June) 1957.

Several antibiotics which were dissolved in water together with vitamins of the B-complex showed a decrease in antibacterial activity.

The formula of the vitamins used was: Aneurin HC1 200 mg., Riboflavin 50 mg., Pyridoxine HC1 30 mg., Cyanocobalamin 30 mcg., Nicotinamide 400 mg., Pantothenic acid 50 mg. They were added to the culture media in four concentrations, i.e., 2%, 0.25%, 0.08% and 0.04%. Two test organisms were used: the Gram-positive *Streptococcus faecalis* M 19 and the Gram-negative *Klebsiella pneumoniae* P.C.I. 602. Nephelometric measurements were carried out in order to assay the antibiotic activity on the growth of the micro-organisms.

No inactivation was seen with chloramphenicol, penicillin and neomycin. Loss of antibacterial activity on *Streptococcus faecalis* was found with chlortetracycline, oxytetracycline, tetracycline, magnamycin, streptomycin, dihydrostreptomycin, tyrothricin, and actinomycin C. Loss of antibacterial activity on *Klebsiella pneumoniae* was found with chlortetracycline, oxytetracycline, tetracycline, magnamycin and erythromycin.

The most evident case was that of the tetracyclines. The inactivation was very intense, being optimum for the 0.25% concentration of vitamin. The inactivation process appeared to be a chemical reaction, not a biological one. The reaction was not instantaneous, but progressive with time.

The factor in the vitamin complex responsible for the inactivation was riboflavin. It was shown, that the inactivation reaction was a photochemical oxidation of the tetracycline molecule, in which riboflavin played the role of a sensibilisator.

The inactivation reaction did not take place in the dark, nor in the presence of nitrogen and a reducing agent, i.e., sodium hyposulfite.

J. WOUTER HUISMAN

STERILIZATION OF AMPULS

The Absorption of Formaldehyde Vapour by Cracked Ampoules. T. D. Whittet, Hosp. Pharm. (Canada) 10:28 (Jan.-Feb.) 1957.

A legal decision has determined that the sterilization of the exterior surface of ampuls of spinal anesthetics with antiseptic solutions can be injurious to patients and this method should not be used. Paralysis has occurred when phenol in such a solution has penetrated the ampuls used for spinal analgesia. Some local analgesics may be autoclaved several times while others will deteriorate when heated. A Ministry of Health Sub-Committee has recommended the sterilization of thermolabile drugs with formaldehyde vapor, although the possibility of penetration of the ampul by the vapor has been suggested.

The Ministry of Health's Sub-Committee investigated one hospital using this method and found the method to be quickly effective against bacterial contaminants. The method consisted of the use of glass containers with tablets of paraformaldehyde placed in the bottom and covered with a layer of slightly moistened lint. The ampuls are placed on the lint and the container closed and sealed with adhesive tape. One hour's exposure is necessary for sterilization of the outside surfaces of the ampuls, with fresh tablets added periodically. The containers, each with only one kind of ampul stored in it, should not be refrigerated. The sub-committee felt that this method of sterilization would help to prevent ampuls from being cracked and the contents thus contaminated.

In an experiment to investigate the amount of formaldehyde which could penetrate cracked ampuls, 24 ampuls each containing 10 ml. of water for injection were subjected to treatment which caused minute cracks in the ampuls. Six uncracked ampuls were used as controls. The cracked ampuls and the controls were stored in accordance with the method described by the Ministry of Health's Sub-Committee. The control ampuls were exposed to the vapor for 24 hours; six of the cracked ampuls were removed after an hour's exposure, and additional groups of six were removed at intervals of 3, 6 and 24 hours. After removal the cracks were sealed with beeswax until the contents of the ampuls could be assayed.

The assays showed a trace of formaldehyde in the ampuls exposed one hour, and measurable quantities in those exposed 24 hours. The controls showed no penetration. Ampuls stored in phenol solutions have shown the same results. It has been postulated that "invisible cracks" or "molecular flaws" could allow penetration of antiseptic solutions, although the author has found no evidence of this in experiments with several hundred ampuls, except in cases where the ampul was cracked.

Artificially-made cracks are not entirely uniform and may cause variation in results. But using this method, results generally show very little contamination after one hour's exposure to formaldehyde vapor, but an appreciable increase in penetration after 3 or more hours.

Bacteriologic tests were made to show the effectiveness of sterilization with formaldehyde vapor and these tests showed that the vapor did sterilize the ampuls. This effectiveness, coupled with the unlikelihood of contamination of the ampul except where gross cracks are evident or when exposed longer than one hour, suggests that formaldehyde vapor for sterilization of ampuls should prove satisfactory. However, the ampuls should not be left in the formaldehyde vapor for more than 1 hour.

JOANNE BRANSON

VOLUME OF DROPS IN PARENTERAL INFUSIONS

Volume of Drops in Parenteral Infusions, Jeanneret, P., Essellier, A. F., and Schneider, E., Pharm. Acta, Helv. 32:118 (March) 1957.

The volume of drops is influenced mainly by two factors: (1) *The infusion set.* Eight drop counters of different (Swiss) makes showed considerable variation in drop size (14.0 - 22.4 drops per cc. at a rate of 60 drops per minute). (2) *The drop rate.* With increasing drop rate (drops per minute) the drops increase in volume. On an average, with a drop rate of 20 drops per minute, there were 19 drops in one cc. against 16 drops in one cc. at a rate of 200 drops per minute.

Dissolved substances appeared to have a relatively small influence on the drop size. For instance, at a drop rate of 60 drops per minute, 20.1 drops of distilled water were necessary for one cc., against 20.2 drops of normal saline, 21.5 drops of 20% invert sugar and 20.8 drops of 10% dextrose.

A nomogram is presented taking into account the variable factors and permitting calculation of the drop rate (drops per minute) corresponding to the infusion rate in cc. per minute.

J. WOUTER HUISMAN

STERILITY OF EYE DROPS

Sterility of Eyedrops, Goettsch, F. J. B., Ophthalmologica 132:167 (Sept.) 1956.

The outbreak of an epidemic of Bacillus pyocyaneus ulcers in an ophthalmological outpatient clinic led to an investigation of bacterial contamination of the eyedrops used.

It appeared that out of eighteen solutions, fifteen were contaminated, including those containing penicillin and albucid. Stock solutions were not infected, so the contamination occurred during use. The eyedrops were reviewed every two weeks, the frequently used ones every 2-3 days. As a result of this investigation, phenylmercuric nitrate (1:25,000) is added to all eyedrops now except normal saline. Zephirol (1:25,000) is added to normal saline as phenylmercuric nitrate attacks in this solution the aluminum caps of the bottles and produces a precipitate. Weekly culturing of eyedrops, as well as hourly sampling, have not revealed any contamination since the disinfectants have been used.

Another investigation was made in the consulting rooms of twelve ophthalmologists. The eyedrops of nine were contaminated with gram-negative or gram-positive bacilli, and gram-positive cocci or fungi. Bacillus pyocyaneus was not found however. Two oculists had sterile preparations. They added 4 drops of chloroform per 10 ml. as a routine measure. One ophthalmologist, who had sterile drops too, renewed his stock every week.

J. Wouter Huisman

VISCOSITY OF SUSPENDING AGENTS

A Study of the Viscosity of Some Suspending Agents, Joslin, R. S. and Sperandio, G. J., Drug Standards 25:72 (May-June) 1957.

Viscosity change is an important factor affecting the rate of sedimentation of a suspension. Acacia, bentonite, sodium alginate, methylcellulose and polyethylene glycol 400 monostearate are the suspending agents used in this study.

Dispersions of each of these substances were prepared with both boiling water and with water at room temperature, and a different portion of each dispersion was stored at room temperature, 40 degrees and 60 degrees.

There was less viscosity change in the dispersion of acacia prepared with boiling water and in the dispersion of sodium alginate prepared with cold water. The temperature of the water used in preparing dispersions of the other three agents was not an important factor in changing the viscosity of these dispersions.

The dispersions of acacia, methylcellulose, bentonite and sodium alginate that were aged at room temperature showed the least change in viscosity. The acacia, sodium alginate, and methylcellulose dispersions became less viscous with aging while the bentonite and polyethylene glycol 400 monostearate became more viscous upon aging.

It was also shown that the pH of the dispersions studied became more acidic upon aging.

Richard Martin

INACTIVATION OF POLIO VIRUS

Immunogenicity of Poliomyelitis Vaccine Prepared with Ultraviolet Irradiation and Mild Heat, Shaughnessy, H. J. et al, Proc. Soc. Exper. Biol. Med. 95:251 (June) 1957.

This paper discusses an experiment designed to show the effects of varying intensities of ultraviolet irradiation with and without subsequent exposure to mild heat on inactivation of poliomyelitis virus (trivalent pools of Type I, II and III) and on antigenicity of the resulting vaccine in animals.

The quantity of ultraviolet energy absorbed per ml. of virus suspension was varied by passing the suspension through a specially designed machine at different rates. Exposure to mild heat was carried out for several days in an incubator set at 37-40°C.

Potency tests of the vaccines were made in mice and monkeys by the methods described in "Minimum Requirements: Poliomyelitis Vaccine"—First Revision, April 12, 1955, by the National Institutes of Health.

It was found that if sufficient ultraviolet energy was used to completely destroy the cytopathogenicity of the virus for monkey kidney cells, the antigenicity of the vaccine would be reduced. However, through a combination of less intense ultraviolet irradiation followed by exposure to mild heat, a non-cytopathogenic suspension of good potency was produced comparing favorably with the antigenicity of formalin control vaccine. A margin of safety between complete inactivation and appreciable loss of antigenicity is therefore made possible through this procedure.

Experience thus far indicates a degree of consistency and reproductibility for the method described, but the reasons for the effectiveness of such a combination in producing a non-cytopathogenic suspension were not elucidated. One hypothesis states that virus particles which are altered or injured by the ultraviolet, but not completely killed, become more rapidly non-cytopathogenic at the incubator temperature.

Theodore Benya

POWDERED OINTMENT BASE

A Simplified, Powdered, Washable Ointment Base, Lee, James A., Caver, Phyllis, and Nobles, W. Lewis, Am. J. Pharm. 129:190 (June) 1957.

A powdered ointment base consisting of a single chemical from which ointments may be prepared simply by adding water, followed by agitation without the use of heat is described. This base meets the general criteria for ointment bases.

Carbopol 934 is utilized for this purpose once it has been preneutralized. This method involves the preparation of a slurry of Carbopol 934 which is then filtered through a Buchner funnel. This yields an adhesive white mass which is dried for about 1½ hours at 125 degrees C. It is then reduced to a fine particle size in a Waring blender.

Utilizing this dried sodium salt of Carbopol a number of ointments were prepared using from 2 to 10% concentrations in water to effect a suitable ointment gel. Twelve agents commonly employed in ointment form were incorporated into ointments using the sodium salt of Carbopol. The dry medicaments were blended with sodium Carbopol and then the ointments were prepared by the addition of water with agitation. The authors report no evidence of changes in the ointments after ninety day storage at room temperature.

Clifton J. Latiolais

MECHANICAL STRENGTH OF TABLETS

Evaluation of the Mechanical Strength of Tablets, Munzel, K. and Kagi, W., Pharm. Acta. Helv. 32:305 (Aug.) 1957.

Two methods were developed for measuring the mechanical strength of tablets. One method concerned the loss caused by rolling the tablets in a specially designed machine, and the other method concerned the binding strength of the tablets.

The "Turbula," a commercially available mixing machine, was used for the evaluation of the loss on rolling. Revolution number, time of rolling and number of tablets in the revolving unit appeared to be influencing factors.

The following method was recommended: Ten tablets are brushed clean of dust, weighed and rolled into Turbula for ten minutes at a speed fo 84.5 revolutions per minute. The tablets are brushed carefully again and weighed. The loss on rolling is defined as the percentage weight loss suffered by the tablets during the rolling test.

The binding strength of the tablets was measured by means of a modified "Dynstat," which otherwise is mainly used for the examination of plastics. With this method it was necessary to manufacture the tablets to be tested in the form of prismatic bodies of definite size, in order to fit into the instrument. Yet since the investigations only aimed at an examination of the internal factors of tablet resistance. (See next abstract), this best met the requirements. The loss-on-rolling test, applied to nine commercial tablets, revealed considerable difference between tablets of different origin. It was proposed that a norm be established

according to which the loss on rolling, as determined by means of the above method, should not exceed 10 percent.

J. WOUTER HUISMAN

MECHANICAL STRENGTH OF TABLETS

Affection of the Disintegration and Mechanical Strength of Tablets by the Form of the Granulate, Munzel, K. and Kagi, W., Pharm. Acta. Helv. 32:321 (Aug.) 1957.

Investigations were carried out with Granulation Simplex Ph. Dan. IX, i.e., a mixture of 30% lactose and 70% potato starch. Pressure and form of tablets were maintained as equal as possible.

Granulates were made in two different ways, i.e., by shaking ("Schuttel granulate") and by pressing ("press-granulate"). The binding agents were a 10% solution of sucrose, a 10% solution of soluble starch, and a 4% solution of gelatin. The glidants used were talc and carbowax 6000. As a lubricant, stearic acid was used.

The disintegration time, the binding strength and the loss on rolling (see previous abstract) of 72 different batches were investigated. The following conclusions were drawn:

Shaken granulates give tablets with a lower binding strength and a larger loss on rolling than the pressed granulates. However, the former's disintegration time is shorter than the latter's.

Sucrose as a binding agent causes the shortest disintegration time, gelatin the longest, with soluble starch in between. Gelatin gave the greatest binding strength to the tablets, soluble starch the smallest loss on rolling.

Talc is superior as a glidant to carbowax 6000, as it has much better influence on disintegration and mechanical resistance of the tablets. Stearic acid had an unfavorable influence on disintegration time and even more so on binding strength and loss on rolling.

J. WOUTER HUISMAN

ACCIDENTAL DRUG POISONING

The Public Health Problem of Accidental Poisoning, Conley, B. E., Am. J. Pharm. 129:87 (Mar.) 1957.

From the mortality statistical report for 1950, nearly 12,000 persons have died from accidental and intentional exposure to harmful chemicals in which 3,353 cases were classified as accidental poisoning and 3,961 cases as suicidal. Drugs contributed from 20 to 25 percent of the fatal and suicidal poisonings. If fatalities from therapeutic overdosages, or liberal self-administration of a drug and drug addiction were considered, the proportion of accidental fatalities due to drugs would have been considerably higher.

Significantly, drugs constituted a minor fraction (0.1 to 0.3 percent) of the total annual production of synthetic organic chemicals; yet it caused a disproportionately high incidence of deaths. The basic factors underlying the facts were attributed (1) to a widespread public casualness and ignorance of the toxicity, handling, and storage of drugs, and (2) to the great availability of drugs and other chemicals capable of causing harm.

The comparative frequency of accidental drug poisoning for various age groups and a breakdown of deaths according to drug categories were tabulated. Salicylates, barbiturates, bromides, opium derivatives, and other analgesic and hypnotic agents were the leading causes of accidental drug fatalities with barbiturates being the chief cause of poisoning in adults and salicylate poisonings occurring the most frequently in the very young (approximately 80 percent among children under five years of age).

Two principal efforts have been made to prevent accidental poisonings, namely, the establishment of poison information and control centers and the development of uniform chemical labeling laws for hazardous products not presently regulated.

NORMAN HO

current literature

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

ADMINISTRATION

—COSTS

Anon.: What It Costs to Use Needles and Syringes, *Modern Hosp.* 89:77 (Sept.) 1957.

—INVENTORY

Oddis, Joseph A.: Perpetual Inventory (Service from Headquarters), *Hospitals* 31:20 (Nov. 1) 1957.

TeKolste, Elton: Cost Control (Service from Headquarters), *Hospitals* 31:20 (Nov. 1) 1957.

—PERSONNEL

Sister Marie: Rx: An Integrated Hospital Team, *Hosp. Progress* 38:88 (Oct.) 1957.

Stauffer, Isabel: Personnel Patterns, *Hosp. Pharm.* (Canada) 10:276 (Sept.-Oct.) 1957.

—PURCHASING

Terenzio, J. V.: Some Legal Aspects of Hospital Purchasing, Part II, Warranties, *Hosp. Management* 84:117 (Nov.) 1957.

Wolf, Earl C.: Competitive Bid Buying, *Hosp. Progress* 38:140 (Nov.) 1957. Reprinted from the *Purchase Exchange* 1:No. 1 (Oct.) 1957.

LIBRARY AND REFERENCE

Flanagan, John J.: The Library is Important to the Whole Hospital, *Hosp. Progress* 38:104 (Nov.) 1957.

Parker, Paul: (Hospital Pharmacists Provide Consultant Service), *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 18:678 (Nov.) 1957.

CENTRAL STERILE SUPPLY

Skolaut, M. W. and Fitzwater, J. L.: Sterile Supply Fits Into the Pharmacy, *Modern Hosp.* 89:98 (Sept.) 1957.

EDUCATION

Anon.: Pharmaceutical Education, *J. Am. Pharm. Ed., Pract. Pharm. Ed.* 18:601 (Oct.) 1957.

Brodie, Donald C.: Pre-Professional Education in Pharmacy, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 18:608 (Oct.) 1957.

Busse, Louis: Pharmacy Internship Training, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 18:612 (Oct.) 1957.

Tice, Linwood F.: The Future of Pharmaceutical Education, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 18:614 (Oct.) 1957.

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Gershenfeld, Louis: The Hospital Pharmacists' Responsibilities In the Production of Parenterals, *Am. J. Pharm.* 129:163 (May) 1957.

PHARMACY AND THERAPEUTICS COMMITTEE
(Includes Formularies)

Berman, Alex: Tradition and Change: The Hospital Formulary in the United States, *J. Mondial De Pharmacie* No. 1:25 (Sept.) 1957.

Editorial: Rational Drug Therapy, *Hospitals* 31:40 (Oct.) 1957.

STATISTICS AND SURVEYS

Moravec, Daniel: Pharmacy Service in Smaller Hospitals, *Hosp. Management* 85:112 (Nov.) 1957.

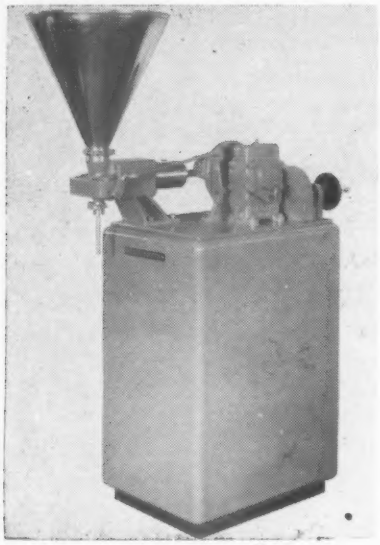
Block, Louis: Prototype Study: Proprietary Hospitals (25 Bed Hospitals) *Modern Hosp.* 89:77 (Nov.) 1957.

Notes and Suggestions

edited by CLIFTON LATIOLAIS

MONO-PISTON FILLING MACHINE

The Kiefer Mono-Piston Filling Machine* is semi-automatic and can be used for filling creams, ointments, thick liquids, etc. All contact parts are made of stainless steel and teflon. It is equipped with a 220V, one-half horse-power motor with a variable speed drive. Two sizes of pistons are available. Number 1 piston can be adjusted



to deliver from ½ ounce to 16 ounces per stroke and Number 2 piston from 2 ounces to 32 ounces per stroke. At usual operating speeds, 60 to 80 dozen jars can be filled per hour. This rate may be increased with small jars to 100 dozen or over per hour. The hopper has a capacity of 7 gallons. Floor space 26″ x 20″, table height, 36″.

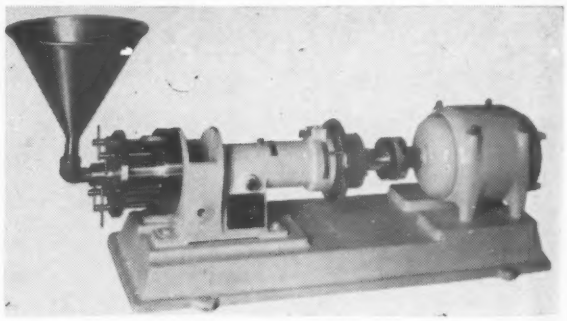
*Karl Kiefer Machine Company, Cincinnati 2, Ohio

FERROUS FUMARATE

A descriptive brochure on ferrous fumarate (Toleron®) has been released by Mallinckrodt Chemical works. Ferrous fumarate provides a readily available source of ferrous iron which can be used alone or as a constituent of various drug preparations for oral administration. Toleron is therapeutically equivalent to other ferrous compounds, such as ferrous sulfate and ferrous gluconate, and offers advantages with regard to tolerance, taste and unusual stability according to the manufacturer.

COLLOID MILL

The Charlotte Colloid Mill Model ND-1* is particularly suited to the processing of ointments, lotions, creams, emulsions, pastes, aqueous suspensions, etc. in the hospital pharmacy. It has a rated capacity of up to 35 gallons per hour. Other models are available with higher production capacities.



The mill is of stainless steel construction and is designed to permit sterilization (by autoclaving) of all parts coming in contact with the material being processed. The external adjustment wheel enables the operator to adjust clearances between rotar and stator to an extremely fine ratio. A uniform particle size is absolutely assured. Model ND-1 is equipped with a one hp motor, rotating at 3600 rpm.

*Chemicolloid Laboratories, Inc., 55 Herricks Road, Garden City Park, New York

SUPPOSITORY MOLDS

A booklet has been issued by Phar-Metic Equipment describing a line of suppository molds which the company has available in this country. Additional information may be obtained by writing Phar-Metic Equipment, South Orange, N. J.

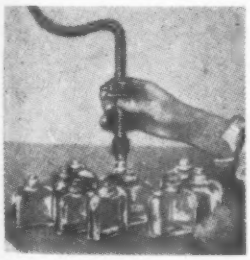
TUBE CRIMPING AND CLOSING MACHINE

Ointment tube crimping and closing machine No. 702* (manually operated) consists of two stations. In the first station tubes are flattened when filled too high and the excess quantity of ointment is pressed out. Then the tube is set in

the closer and crimper by turning the hand lever back and forward. One fold and crimp is made each time the hand lever is brought forward and backward. Current price is $110.00 f.o.b. Brooklyn.

*Perl Machine Manufacturing Company, 68 Jay Street, Brooklyn, New York

HAND FILLING VALVE



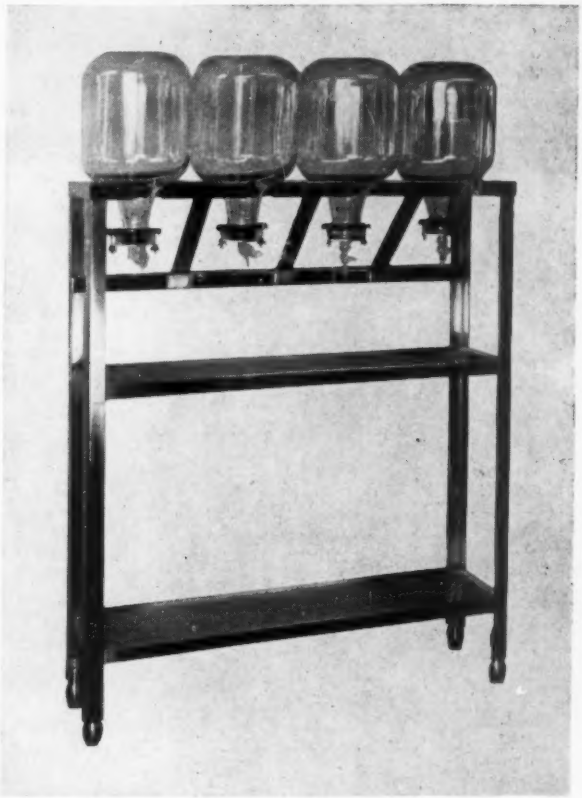
The automatic hand filling valve Types "A" and "B"* can be used with either gravity, vacuum or pressure operations. The valve spout is inserted into the bottle and, upon depressing the valve, liquid starts flowing. Liquid levels in bottles are set and controlled by means of a thumb-screw adjustment on spout. Excess liquid goes through the overflow tubing into a receptacle. Upon lifting valve from bottle top, flow of liquid stops automatically. Type "A" valves are available with interchangeable filling spouts.

Type "B" valves have a shut-off on the spout making them suited for filling viscous, oily, and foamy solutions. Filling is guaranteed dripless. Type "B" valves do not have interchangeable filling spouts.

*Perl Machine Manufacturing Company, 68 Jay Street, Brooklyn 1, New York.

CARBOY RACK

Model 1070* Carboy Rack is designed for storage and dispensing of bulk pharmacy fluids. The rack accommodates 4 five-gallon carboys and has a filling shelf 20 inches below the carboy support section. The lower shelf may be used for storage of reserve carboys.



The rack is made of heavy gauge Type 316 stainless steel in either tubular or angle-iron construction and polished to a No. 4 bright finish. Overall dimensions are 48″ long x 60″ high x 12″ deep. Current price is $295.00 each, or approximately $250.00 in lots of two or more.

*Macbick Co. 243 Broadway, Cambridge, Mass

PRESERVATIVES FOR GLYCERIN SOLUTIONS

Although concentrated glycerin is resistant to bacteria and microorganisms, formulations containing low concentrations of glycerin sometimes require preservatives. A combination of 0.07 percent methyl parahydroxybenzoate and 0.03 percent propyl parahydroxybenzoate is suggested for foods and internal medications. Data sheets on these and other preservatives are available from Chemo Puro Mfg. Corp., 150 Doremus Ave., Newark 5, N. J.

ASHP affiliates

Southern California Society

Members of the Southern California Society of Hospital Pharmacists met at the Mt. Sinai Hospital in Los Angeles for the September meeting. The principal speaker, Dr. Lucien Guze, presented a talk on "Treatment of Urinary Tract Infections." Dr. Guze, who carries out clinical investigations for the Veterans Administration, is also an Assistant Clinical Professor at the University of California, Los Angeles.

Another highlight of the meeting was the timely discussion on the Asian influenza vaccine. The subject was opened with a history of influenza epidemics and the types of vaccines available. This was presented by Mr. Wendell Hill, Chief Pharmacist at Orange County Hospital.

During the business session, Mr. Charles Towne, Director of Pharmacy Service at the Los Angeles Veterans Administration Center, was named delegate to the Pan-American Congress on Pharmacy and Biochemistry which is being held in Washington in November. Other committees were appointed and reports were received during the business session.

Northeastern New York Society

The initial function of the Northeastern New York Society of Hospital Pharmacists for the 1957-1958 season was an educational trip to E. R. Squibb and Sons in New York and New Jersey. Thirty members and guests arrived at the Hotel Abbey on Sunday afternoon, September 22. Following dinner that evening, John R. Kenny, Jr., Assistant Manager, Trade Distribution, spoke to the group. Later that evening the entire group enjoyed a fine show at the Radio City Music Hall.

On Monday, the group was taken to the New Brunswick Laboratories to view the manufacturing and laboratory operations under the direction of Ross Blue. After dinner on Monday evening, Dr. Gilbert Cyr spoke on "Problems Involving Pharmaceutical Preparations." On Tuesday the group visited the impressive IBM operation in New York City.

Greater St. Louis Hospital Pharmacists

Members of the Hospital Pharmacists' Association of Greater St. Louis met at the St. Louis County Hospital on Tuesday evening, September 10. In the absence of the President, Vice-President Joseph Guller presided. During the business session there was considerable discussion regarding membership in the group and attendance at the meetings. Several possibilities were suggested and efforts are being made to stimulate participation.

The principal feature of the meeting was a film on "Sterilization Procedures," which was made available by Winthrop Laboratories.

Colorado Society

"Narcotic Controls in the Hospital" was the principal subject presented at the September 17 meeting of the Colorado Society of Hospital Pharmacists. The speaker, Mr. Frank A. Sojat, District Supervisor of the Bureau of Narcotics, pointed out six important reasons for keeping records on narcotics. The discussion was followed by a question and answer period. Included also as part of the program was a film on "Narcotic Addiction," which is available from Winthrop Laboratories.

During the business session, committee appointments were made and tentative plans were announced in connection with adopting a Constitution and By-Laws with plans for affiliating with the national organization.

Northern California Society

The 108th meeting of the Northern California Society of Hospital Pharmacists was held at St. Joseph's Hospital in San Francisco on September 10. The guest speaker, Dr. Frederick Meyers of the University of California, addressed the group on "Human Requirements in Vitamins." He emphasized recent experimental studies which indicate that the adult nutritional needs in vitamins are much less than the popular daily requirement figures. Dr. Meyers confined the discussion to nutritional rather than the therapeutic aspects of vitamins except to point out the fact that patients taking isoniazid can suffer from B_6 depletion and should receive 25 to 50 mg. daily while taking the drug.

During the business session reports from committees were presented and plans were outlined for future meetings.

New members of the Northern California Society introduced included Robert E. Olson of Peninsula Hospital, Burlingame; Yuriko Ishizuka of Peninsula Hospital, Burlingame; John J. Eiler of the School of Pharmacy, University of California, San Francisco; Lorraine M. Brocco, University of California Hospital Pharmacy, San Francisco; and Irene I. Boyle of Levine Hospital, Hayward.

Western Pennsylvania Society

Members of the Western Pennsylvania Society of Hospital Pharmacists attended their Third Annual Seminar on October 23 and 24, 1957. The program participants included such prominent personages as:

Sister Mary John, R. S. M., Chief

Pharmacist, Mercy Hospital, Toledo, Ohio, and recent recipient of the H.A.K. Whitney Award; Mr. Herbert L. Flack, Director of Pharmacy Services, Jefferson Medical College Hospital, Philadelphia, Pa.; Mr. Norman N. Baker, Apothecary-in-Chief, The New York Hospital, New York City, N.Y.; and Mr. Walter Frazier, Chief Pharmacist, Springfield City Hospital, Springfield, Ohio.

The Seminar opened on Wednesday evening, October 23, 1957, at St. Francis General Hospital and Rehabilitation Institute. Mr. Herbert Flack presented the first address, entitled "Ways to Improve Hospital Pharmacy Service."

On Thursday, October 24, 1957, both the morning and afternoon sessions were held at the Western Pennsylvania Hospital. Mr. Walter Frazier addressed the group on "The Utilization of Non-Professional Personnel in Pharmacy;" Sister Mary John, on "A Combination Pharmacy-Central Supply in Action;" and Mr. Norman N. Baker on "Applying Work Simplification to Hospital Pharmacy."

The final evening session, held at St. Francis General Hospital and Rehabilitation Institute, included a panel, composed of our four guest speakers, President Gerard J. Wolf as moderator, and an actively participating audience. The subject—Hospital Pharmacy Problems—created a lively discussion.

A successful seminar concluded with refreshments and a social hour.

Michigan Society

The Michigan Society Pharmacists met at University Hospital in Ann Arbor on October 17. In the absence of President Max Miller, the meeting was presided over by Mr. Edward Superstine. Following a brief business session, the group saw a demonstration on "Aseptic Technique in the Preparation of Sterile Solutions." This was presented by Mr. John Lucasse and Mr. Theodore Benya, senior interns at University Hospital.

Greater Kansas City Society

Fourteen members of the Society of Hospital Pharmacists of Greater Kansas City met at the Blue Cross-Blue Shield Building on September 11. This being a business meeting, the principal items covered included revision of the Constitution and By-Laws, working with the Administrative Council of the Kansas City Area Hospital Association in connection with increasing active membership in the Kansas City group, and participation in the disaster planning in the area.

Participants in the Third Annual Seminar of the Western Pennsylvania Society. Left to right: Sister Mary John, Herbert L. Flack, Gerard J. Wolf, Norman N. Baker, and Walter Frazier.

Greater New York Chapter

Members of the Greater New York Chapter of the ASHP met at St. Catherine's Hospital in Brooklyn on October 15. Following committee reports and the general business session, officers for the coming year were elected. These include *President,* Sister M. Virginia, Mercy Hospital, Rockville Center, Long Island; *Vice-President,* Sister M. Nicodema, St. Peter's Hospital, Brooklyn; *Treasurer,* Sister M. Donatus, St. Clare's Hospital, New York City; *Corresponding Secretary,* Sister M. Rose Dominici, St. Catherine's Hospital, Brooklyn; and *Recording Secretary,* Sister Maria Joseph, St. Joseph's Hospital, Far Rockaway.

During a general discussion, the members considered various projects which they plan to undertake this season. Much interest was shown regarding plans for the Hospital Pharmacy Seminar which is scheduled during the fall.

Dade County Society of Hospital Pharmacists

The Dade County Society of Hospital Pharmacists (Miami, Florida) held a Seminar at Mt. Sinai Hospital in Miami Beach on Saturday, September 14. Following registration and a welcome by Mr. Gertner, Executive Director of Mt. Sinai Hospital, the following program was presented:

"The Hospital Pharmacist's Role in the Asiatic Influenza Situation," by I. Goldberg, Chief Pharmacist, North Shore Hospital.

"Investigational Drugs and How They Should Be Regulated," by Carl Dell, Director Pharmacy Service, Jackson Memorial Hospital.

"Sources of Information for the Hospital Pharmacist," by Eleanor Morgan, Pharmacist, Mt. Sinai Hospital.

"The Physician and the Hospital Pharmacist," by Dr. Andrew J. Leon.

"Research and Pharmacology," by Dr. William B. Deichman, University of Miami Medical School.

"The Administrator and the Hospital Pharmacist," by Mr. Samuel Zibit, Assistant Director, Mt. Sinai Hospital.

Utah Society

The July business meeting of the Utah Society of Hospital Pharmacists was held on July 27 at the Utah Valley Hospital in Provo. Mr. William Wilcox, Chief Pharmacist, acted as Host and conducted the group on a tour of the new wing of the hospital which is now under construction. A new pharmacy will be included in the much needed increase of space.

Mrs. Nellie Vanderlinden, Chief Pharmacist at the Latter Day Saints Hospital in Salt Lake City, reported on the Seattle Institute which she recently attended.

as the president sees it

LEO F. GODLEY

Bronson Methodist Hospital
Kalamazoo, Michigan

We were saddened indeed by the death of Dean Edward Spease on October 12. As some of you know, he was Dean at Western Reserve University when my wife and I were graduate students there. We shall miss the Christmas cards that came each year; and the cheerful notes he always wrote when we had a new baby at our house. In hospital pharmacy his name will live on as a pioneer. Whenever we hear of hospital pharmacy graduate study programs, of formulary systems, of minimum standards, of internships . . . his name will be remembered.

Oklahoma was a nice place to visit. I met with the Oklahoma Society in Norman. They had a very fine program and the group was very enthusiastic. Sister Teresa is their President and it was good to see her operate in her official capacity. She gets a great deal of cooperation and it's easy to see why. The two schools in Oklahoma were well represented and I got to meet Professor Bienfang who wrote about "Gnafneib." I was particularly sorry that Dean Strother (an old professor of mine), of Southwestern College of Pharmacy, was not able to get to the meeting, although two members of his staff were present.

Early in October, I went to the American Hospital Association Convention and participated on a panel on the Formulary System. It was an honor and a pleasure to discuss with such practitioners as Sister Mary Etheldreda, Dr. August Groeschel, Dr. Don Francke, Dr. Robert Cadmus, and Judge Victor Hansen. It was a satisfying experience and I hope that there were some administrators in the audience.

On October 5, I met with the Board of Selections of the Research and Development Committee in New York City. They had a heavy day's work; and it was most encouraging to see the interest among hospital pharmacists in developing research programs in the hospital pharmacy. We are fortunate to have Drs. Glenn Jenkins, Don Skauen, and Arthur Purdum to evaluate these requests. Their participation, when translated in terms of service to the SOCIETY is a commodity that transcends things that are purchasable.

I met with the Wisconsin Society of Hospital Pharmacists on October 17, in Milwaukee. The University Extension Services in Pharmacy in cooperation with the Wisconsin Society turned out a very successful one-day institute. President Richard Henry worked very hard; and a most commendable job with the organizing particulars was evident. It was good to see old friends like Sister Gladys Robinson and Paul Bjerke again. I had a tour of Sister Gladys' Department at Milwaukee General and I would urge all of you to stop by and pay her a visit when you're passing through Milwaukee.

I have enjoyed attending the Pfizer seminar programs that have been sponsored in conjunction with local groups. I think this effort from industry has done a great deal for the SOCIETY and I congratulate Burns Geiger of Pfizer Laboratories for maintaining a constantly pleasing and compatible relationship with our organization.

In the month of October, I had two Pfizer seminar appointments—Oklahoma and Oregon. I was ill and missed the Oregon date; but on a two-hour notice, I called Don Francke and asked him if he would fill in for me in Portland. Luckily, Don's schedule was such that he could see his way clear to go. Thus, I feel that I was able to do a very good deed for Oregon in making Dr. Francke available to them. Incidentally, Don told me that he enjoyed the trip, the meeting, and the banquet; and I was very happy that I could delight the hospital pharmacists of Oregon from my sick bed!

I consider myself a fortunate president in being able to represent our organization at the Fourth Pan-American Congress of Pharmacy and

Biochemistry in Washington, D. C. (Nov. 3-9). It was a great thrill to participate in this meeting with pharmacists from all the Americas. Though thinking scientifically and professionally through the medium of simultaneous interpretation is a bit frustrating, the barrier presented by four languages was greatly broken by this facility.

The Hospital Pharmacy Section of the Congress was quite appropriately administered by Secretary Grover Bowles and we were pleased with the Chairman of our section, a hospital pharmacist from Cuba—charming and gracious Dr. Margarita Tomargo.

We were happy that we were able to extend some personal hospitality to hospital pharmacists who lived in the other American countries. We felt that we got to know each other pretty well; and I am sure that everyone is now looking forward to the Fifth Pan-American Congress in Santiago, Chile in 1960.

We sent a letter over my signature the first of November which was intended to inform the membership of the status of our discussion with representatives of the National Pharmaceutical Council. We are reproducing it here for your reference. I'd like to hear from you if you have any comments or suggestions in this regard.

My very best wishes to everyone for a happy holiday season!

To: Members of the American Society of Hospital Pharmacists

As you remember, it was announced at our Annual Meeting last April in New York that the American Society of Hospital Pharmacists had established committee liaison with the National Pharmaceutical Council. This was done at the request of the Council because the Society had objected to the publicity instigated by the Council regarding substitution and the formulary system in hospital pharmacy. You probably also remember that a resolution was passed requesting that the membership be kept informed of the progress made in discussions with the Council. This communication, therefore, is intended to serve that purpose.

An exploratory meeting of the special committee from the N.P.C. and the A.S.H.P. was held in New York City on July 12th. A second meeting was held in Atlantic City on October 4th and 5th. The enclosed release to the pharmaceutical press will give you the names of the participants at the Atlantic City conference as well as a list of the formal presentations made at the meeting.

The Society's committee felt that the reason for industry's objection to the formulary system stemmed from an unfortunate accumulation of misconceptions and misinformation. Accordingly, our approach was planned on frank and forthright dicussion in order to synthesize a more realistic appreciation of the situation. Our intention was to effect a broad mutual understanding, rather than reach an agreement; and to provide a basis for the two groups to work together. In view of the importance of this matter to hospital pharmacists, and its significance in the philosophy of the practice of pharmacy in hospitals, I am happy to be able to report to you that we have achieved, through these discussions, a deeper appreciation by the professional representatives of industry of the value of the formulary system to hospitals. Further, it is apparent to your Society representatives, that we should be cognizant of the problems facing industry relative to the distribution of drugs in hospitals.

We owe a great deal of thanks and appreciation to the working members of this committee for their effective and definite plans for future activity, the committee will continue to function on an 'on call' basis. We urge every hospital pharmacist to study very carefully with his Pharmacy Committee the operation of the formulary system and the distribution of drugs in his hospital. These programs in medical staff government and hospital pharmacy operation are vital forces in the harmony of professional relations and patient care.

Leo F. Godley

LEO F. GODLEY, *President*

NEWS

Dean Edward Spease

Dean Edward Spease, who made outstanding contributions to the specialty of hospital pharmacy, passed away Saturday, October 12, in Akron, Ohio. Memorial services were held in Christ Church Episcopal Church in Hudson, Ohio, on Saturday, October 19th. Dean Spease was an Honorary Member of the SOCIETY.

For 24 years Mr. Spease served as dean of Western Reserve University School of Pharmacy where he established the first graduate program in hospital pharmacy. He is credited with the development of the first set of Minimum Standards for the practice of pharmacy in hospitals which was adopted by the American College of Surgeons in 1936, as criteria for the evaluation of pharmacy services in hospitals. He advocated the establishment of hospital pharmacy internships, the use of a formulary in hospitals, and the establishment of a Pharmacy and Therapeutics Committee.

Dean Spease was recognized for his work in hospital pharmacy by having conferred upon him an honorary Master of Science degree from the Philadelphia College of Pharmacy and Science in 1936 and by having been made an honorary member of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS in 1946. He was presented with the H.A.K. Whitney Award by the Michigan Society of Hospital Pharmacists in 1952 to further distinguish him for his contribution to hospital pharmacy.

Mr. Spease received his undergraduate degree in 1905 from Ohio State University, where he served as an instructor for six years and as an assistant professor for two years before being named to the deanship at Western Reserve in 1916. He was a former president of the American Association of Colleges of Pharmacy and held membership in the American Pharmaceutical Association, the Ohio State Pharmaceutical Association, the American Association for the Advancement of Science and the Cleveland Academy of Pharmacy and Medicine.

During his retirement, for the past several years, Dean Spease lived at 12 John Clarke Lane in Hudson, Ohio, where he carried on an active correspondence with his many friends in pharmacy. His ideas and enthusiasm for hospital pharmacy were an inspiration to young people in the development of pharmaceutical services in many of the nation's leading hospitals.

Dean Spease is survived by his widow and a brother. He was 74.

Because of Dean Speases' contribution to hospital pharmacy, the ASHP Executive Committee is giving consideration to proposals for giving special tribute to him.

A.H.A. Convention

"Pharmacy" and "Pharmacists" had rightful places in the Annual Convention program of the American Hospital Association meeting in Atlantic City, September 30-October 3. This was not only evident by the number of pharmacists attending the meeting but participation in the various aspects of the Association's activities was noted throughout the program.

In at least two of the sixty-eight round tables designed to assist in specific problems in hospital departments, some phase of pharmacy activity was the major discussion. These included a round-table on "Pharmacy Service in the Smaller Hospitals," in which Mr. Joe Vance, Administrator, South Highlands Infirmary, Birmingham, Alabama, served as Chairman. Mr. Vance is also a pharmacist. Discussants on the panel included J. William Eddy, Administrator, Greenville Hospital, Greenville, Pennsylvania; Frank E. Kunkel, Retail Pharmacist, Kunkel Apothecary, Cincinnati, Ohio; and Daniel F. Moravec, Director of Pharmacy Service, Lincoln General Hospital, Lincoln, Nebraska. On another round table under the subject "Formulary Systems in Hospitals," Dr. Robert R. Cadmus, Director, North Carolina Memorial Hospital, University of North Carolina, led the discussion. Panel participants included Don E. Francke, Director of Pharmacy Service, University Hospital, Ann Arbor, Michigan; Leo F. Godley, Chief Pharmacist, Bronson Methodist Hospital, Kalamazoo, Michigan; August H. Groeschel, Associate Director of Professional Services, The New York Hospital, New York City; Sister Mary Etheldreda, F.S.S.J., Chief Pharma-

cist, St. Mary's Hospital, Brooklyn, New York; and Judge Victor Hansen, Assistant Attorney General, Department of Justice, Washington, D.C. Both of these panels offered an opportunity for stimulating discussions and were attended by hospital administrators as well as pharmacists.

There were also numerous other round table discussions which were of considerable interest to pharmacists. Among these might be included one on "What Is the Future of Prepackaged Items," and "Radioisotope Facilities for the Hospital."

Those attending the Convention also had an opportunity to participate in the Association's House of Delegates and the six General Assemblies, where distinguished speakers covered subjects such as—The Hospital and Education and the Nation; the Hospital and an Informed Public; the Hospital and the Health of the Nation; the Hospital and the Spiritual and Moral Implications of our World; the Hospital and Government and Health; and, finally, the Future of the Hospital.

Hospital pharmacy was also represented among the educational exhibits with a display from the Division of Hospital Pharmacy. Under the direction of Mr. Paul Parker, Director of the Division, the booth served as a center for providing information to hospital administrators. Members of the New Jersey Society of Hospital Pharmacists were in attendance at the booth throughout the week and were most helpful to administrators and pharmacists seeking services of the Division.

Also, of particular note to pharmacists, is the fact that the President-Elect of the A.H.A., Mr. Ray Amberg, holds a pharmacy degree and was once a pharmacist at the University of Minnesota Hospital. Mr. Amberg is presently director at the same institution.

Texas Seminar

The 10th Annual Hospital Pharmacy Seminar sponsored by the Texas Society of Hospital Pharmacists in cooperation with the Pharmacy Extension Service of the University of Texas, will be held in Austin on Saturday and Sunday, February 15 and 16. A meeting of the executive council of the Texas Society will meet at the Stephen F. Austin Hotel on Friday night, February 14 followed by a meeting of the Texas Society.

Registration for the Seminar will start on Saturday morning in the University of Texas College of Pharmacy Library. The tentative program as announced by Mr. Joe Arnette, Director of the Pharmacy Extension Service, is as follows:

SATURDAY, FEBRUARY 15, 1958

8:30 - 9:00 A.M.	Registration.
9:00 - 9:40 A.M.	Invocation and Greetings.
9:40 - 10:30 A.M.	Relationship of the American Hospital Association to Hospital Pharmacists.
10:30 - 10:50 A.M.	Coffee.
10:50 - 11:45 A.M.	Panel: Interprofessional Relationship Between Hospital and Retail Pharmacists.
11:45 - 12:00 Noon	A "Herb Flack" Special.
12:00 - 1:30 P.M.	Lunch, University of Texas Tea House.
1:30 - 2:30 P.M.	Workshops.
2:30 - 3:30 P.M.	Talk by Herb Flack
3:30 - 3:50 P.M.	Coffee.
3:50 - 4:45 P.M.	Panel: Legal Liabilities of Hospital Pharmacists.
4:45 - 5:00 P.M.	A "Herb Flack" Special.
6:45 P.M.	Dinner.

SUNDAY, FEBRUARY 16, 1958

8:00 A.M.	Texas Society of Hospital Pharmacists meeting, College of Pharmacy.
9:00 - 10:00 A.M.	Talk on Pharmacology.
10:00 - 10:20 A.M.	Coffee.
10:20 - 11:10 A.M.	To be announced later.
11:10 - 11:45 A.M.	Pre-packaging.
11:45-12:00 noon	Herb Flack Special.
12:00 - 2:00 P.M.	Lunch—Talks on History of Seminars.
2:00 - 3:00 P.M.	Workshop continued. Report of Group Leaders.
3:00 - 3:15 P.M.	Presentation of Awards.
3:15 P.M.	Coffee for the Road.

The Program Committee is headed by Mr. Robert Lantos, University of Texas Medical Branch, Galveston, along with Fred Borth, President of the Texas Society of Hospital Pharmacists, Austin, and Adela Schneider, Chief Pharmacist at the Southern Pacific Hospital in Houston.

Program On Normal and Abnormal Aspects of the Skin To Be Featured at A.A.A.S. Meeting

The Committee on Cosmetics of the American Medical Association in co-sponsorship with the Society for Investigative Dermatology will present a two day symposium entitled "The Human Integument—Normal and Abnormal." This program has been arranged at the invitation of the American Association for the Advancement of Science and will be presented before the Medical Sciences Section at the Association's 124th annual meeting in Indianapolis, Indiana on December 28 and 29, 1957.

The symposium will be divided into 4 major sessions: I. The Integument as an Organ of Protection; II. Circulation and Vascular Reactions; III. Sebaceous Gland Secretion; and IV. Pathogenetic Factors in Pre-malignant Conditions and Malignancies of the Skin.

Dr. Stephen Rothman, Chicago, will serve as chairman of the symposium. Speakers will include: Dr. Irvin H. Blank, Boston; Dr. Robert D. Griesemer, Boston; Dr. Richard B. Stoughton, Cleveland; Dr. Benjamin W. Zweifach, New York; Dr. Allan C. Burton, London, Ontario; Dr. Robert R. Kierland, Rochester, Minn; Dr. Allan Lorincz, Chicago; Dr. Eugene Van Scott, Bethesda; Dr. Marion B. Sulzberger, New York, Dr. Raymond R. Suskind, Cincinnati; Dr. A. Wesley Horton, Cincinnati; Dr. Herman Pinkus, Monroe, Mich.; and Dr. Frederick D. Malkinson, Chicago.

Further information on the symposium may be obtained by writing to Mrs. Veronica L. Conley, Secretary, Committee on Cosmetics, American Medical Association, 535 N. Dearborn, Chicago 10, Ill.

P.H.S. Releases New Publication

The Public Health Service recently released a new illustrated publication on disease of blood vessels of the brain, third ranking cause of death in the United States.

Strokes and other effects of cerebral vascular disease caused an estimated 179,110 deaths in 1956. Approximately 2 million people are incapacitated or handicapped by brain blood vessel disease, the booklet states.

Dr. James Watt, Director of the Public Health Service's National Heart Institute, which prepared the publication, said that many persons suffering from cerebral vascular disease can be restored to near-normal lives.

"Strokes have been too greatly feared and misunderstood," he said. "The booklet encourages a hopeful, constructive attitude by presenting simple understandable facts about cerebral vascular disease, its causes and effects, and what can be done about it. With proper care and treatment, 9 out of 10 of its victims can be taught to walk again and 3 out of 10 can be restored to gainful work."

The booklet shows the 5 important ways in which vessel disease impairs the working of the brain and outlines steps involved in treatment and rehabilitation.

"Cerebral Vascular Disease and Strokes" is Public Health Service Publication Number 513. A free copy may be obtained from the Heart Information Center, National Heart Institute, Bethesda 14, Maryland.

NEW MEMBERS

NOVEMBER 1, 1957

The following ASHP members sponsored the New Members listed in this issue of THE BULLETIN. *The officers of the* SOCIETY *and the Committee on Membership and Organization appreciate the efforts of the individuals who have encouraged New Members to join the national organizations. Sponsors will be listed along with the New Members in each issue of* THE BULLETIN.

Ardueser, Gloria A.
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Setaro, Joseph J., Jr., 20-56 47th St., Lond Island City (A)
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Jackson, Lee A., Jr., 8414 Cedar Ave., Cleveland
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Lister, Alan L., Jefferson Hospital, Philadelphia

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McNeill, Catherine, 999 Monroe, Apt. 611, Memphis
Smith, Harold F., 123 N. White Station Rd., Memphis (A)

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Miner, Lewis C., 117 Montez Rd., San Antonio
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Verbofsky, Hyman, 302 Reservoir Rd., Beckley
Whitt, Burl J., No. 7 M & S Court, Williamson

FOREIGN

Quashie, John K. A., Station Rd., P. O. Box 2309, Accra, Ghana, West Africa (A)

POSITIONS

in hospital pharmacy

POSITIONS WANTED

CHIEF PHARMACIST—Available in January, 1958; prefer small general hospital, but will consider larger hospital; prefer Michigan, but will consider remainder of Midwest. Two years' experience in hospital pharmacy. For further information write PW-10, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington 7, D.C.

PHARMACIST—female; experience in both hospital pharmacy and retail pharmacy. Prefer southwest or mid-Atlantic area. For further information, write PW-11, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington, 7, D.C.

CHIEF PHARMACIST—prefer general hospital in Florida; registered in Ohio and Florida; experience in both hospital and retail pharmacy work. For further information, please contact the Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W. Washington, 7, D.C., attention: PW-12.

CHIEF PHARMACIST—(or Assistant Pharmacist at large hospital); prefer vicinity of St. Louis; presently employed as staff pharmacist at hospital; registered in Missouri. For further information, please write PW-13, the Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W. Washington, 7, D.C.

CHIEF PHARMACIST—Available approximately November 10, 1957; master's degree in hospital pharmacy, with internship, 1957; experienced in hospital pharmacy. For further information, please write PW-14, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W. Washington, 7, D.C.

CHIEF PHARMACIST—prefer Minnesota or California, with registration in those states; 10 years' experience with the government service, including commissions in U. S. Public Health Service and in the Navy; experience with the Veterans Administration as chief pharmacist; Ph.D in Pharmacy, 1957. For further information, please write the Division of Hospital Pharmacy, PW-15, 2215 Constitution Avenue, N. W., Washington, 7, D.C.

PHARMACIST—registered in Virginia and Tennessee; single and have completed military service. Experienced in retail pharmacy, but am interested in career in hospital pharmacy. For further information, please write PW-16, Division of Hospital Pharmacy, 2215 Constitution Avenue N. W., Washington, 7, D.C.

PHARMACIST—New Jersey registration; prefer Pennsylvania, Florida, Washington, D.C., or Virginia; experience in managing retail pharmacy. For further information, write PW-18, Division of Hospital Pharmacy, 2215 Constitution Avenue N.W., Washington, 7, D.C.

CHIEF PHARMACIST OR CHIEF PHARMACIST-PURCHASING AGENT—prefer non-sectarian and non-governmentally-connected institution of up to 200-bed capacity or larger; presently employed, but available on or before October 15, 1957; experience in both retail and hospital pharmacy. For further information, write PW-19, Division of Hospital Pharmacy, 2215 Constitution, N.W., Washington, 7, D.C.

PHARMACIST—Registered in Illinois and Missouri; six years' experience in hospital pharmacy; some experience in retail pharmacy; desires immediate location. Write PW-20, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, D. C.

CHIEF PHARMACIST IN A TEACHING HOSPITAL—registered in Indiana, Michigan and Missouri; prefer general hospital in Midwest; experience in teaching and in hospital pharmacy; experience includes present position as Chief Pharmacist. For further information, please write PW-26, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D.C.

STAFF PHARMACIST—prefer general hospital in North, East or West; experience in retail pharmacy (1½ years); registered in Texas. For further information, please write PW-25, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D.C.

PHARMACIST—registered in Ohio since 1934; experience in retail pharmacy only (23 years experience); For further information, please write PW-27, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D. C.

PHARMACIST—prefer vicinity of Chicago; registered in Illinois, presently employed there; graduate of the University of Illinois College of Pharmacy. For further information, please write PW-31, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington, 7, D. C.

PHARMACIST—1957 graduate of Xavier University College of Pharmacy; all experience has been in retail pharmacy, but desires to enter field of hospital pharmacy. For further information, please write PW-30, Division of Hospital Pharmacy, 2215 Constitution Avenue N. W., Washington, 7, D. C.

CHIEF PHARMACIST, OR ASSISTANT PHARMACIST IN MEDIUM-SIZE HOSPITAL—registered in Indiana, Michigan and Wisconsin; experience as chief pharmacist, 6 years; experience as purchasing agent and pharmacist, 2 years; prefer Midwest or East. For further information write PW-32, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, D. C.

CHIEF PHARMACIST OR ASSISTANT CHIEF PHARMACIST—presently completing two-year graduate study and internship program for M. S. in Pharmacy. Available after February, 1958. Please contact PW-36, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington 7, D. C.

PHARMACIST IN LARGE TEACHING HOSPITAL OR ADMINISTRATOR—Registered in Ohio; experience in retail pharmacy, hospital administration and X-ray. For further information, please write PW-37, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

STAFF PHARMACIST—B. S. Massachusetts College of Pharmacy; age 27; registered in Massachusetts and New Hampshire; 4 years experience before becoming registered and 4 years in store with large prescription volume. Write PW-35, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

PHARMACIST—Graduate of Medical College of Virginia; age 26; served two years in Marine Corps; managerial experience. Write PW-45, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

HOSPITAL PHARMACY INTERN—Graduate of University of Washington; age 25; presently completing military requirements; prefer northwest. Write PW-46, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

CHIEF OR ASSISTANT CHIEF PHARMACIST—M.S. degree in hospital pharmacy; age 25; any section of country; experience in all phases of hospital pharmacy; completing military service February 15, 1958. Write PW-47, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

STAFF PARMACIST—Graduate Howard University College of Pharmacy in 1957; age 31; limited experience, but anxious to learn; any location. Write PW-50, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

PHARMACIST OR CHIEF PHARMACIST—Graduate State University of Iowa; some hospital pharmacy experience; extensive managerial experience; registered in Illinois and Iowa. Write PW-53, Division of Hospital Pharmacy 2215 Constitution Avenue, N. W., Washington, D. C.

STAFF PHARMACIST—Graduate George Washington College of Pharmacy; age 38; extensive retail pharmacy experience, but would prefer a career in hospital pharmacy; prefer Washington, D. C. or Florida areas. Write PW-52, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

STAFF PHARMACIST—B. S. degree, Howard University, 1957; age 24; male. D. C. registration. Write PW-43, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D. C.

CHIEF PHARMACIST—300 plus bed-hospital, general, preferred; completed Hospital Pharmacy internship; registered in Pennsylvania and Texas; age, 25, male. Completed service requirements. PW-55, Division of Hospital Pharmacy, Washington, 7, D.C. (2215 Constitution Avenue, N.W.)

STAFF PHARMACIST—desires position in East. Male; single; graduate of P.C.P.; two years' graduate study, Northwestern University; three years' experience at University of Chicago Clinics. Write PW-57, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D.C.

CHIEF PHARMACIST—In small hospital, or assistant chief pharmacist or staff pharmacist in large hospital; southwest preferred. Complete internship in February, 1958; graduate, Southwestern State College; registered in Oklahoma. Write PW 58, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D. C.

CHIEF PHARMACIST—any location; single male, aged 29; M. S. in Hospital Pharmacy, University of Michigan; completed service requirements. Write PW-59, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D. C.

POSITIONS OPEN

STAFF PHARMACIST—registered; for manufacturing or dispensing in large teaching hospital; excellent equipment; good hours; 2 weeks vacation; sick leave. Minimum starting salary $425 per month; higher salary for those experienced in manufacturing. Write PO-1, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D. C.

CHIEF PHARMACIST—650 bed hospital, the largest voluntary hospital specializing in the treatment of long-term illness. Growing institution presenting a major challenge to a pharmacist interested in both administration and pharmacology. Write PO-2, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D.C.

STAFF PHARMACIST—132-bed hospital; 40-hour week; salary open. Hospital experience preferred. Write PO-4, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D.C.

ASSISTANT PHARMACIST—eligible for licensure in New Jersey; 350-bed hospital. Write PO-6, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington, 7, D. C.

PHARMACIST—360-bed hospital; large outpatient department, 40-hour week; 6 days' sick leave; 7 holidays per year; two weeks' vacation. Salary dependent upon qualifications. Write PO-8, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington, 7, D. C.

PHARMACIST—92-bed modern hospital; 6 years old; located in town of 11,000 in Pacific Northwest. Starting salary $400 per month, with automatic increases for three years. Write P. O.-10, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

PHARMACIST—80-bed hospital; full responsibility for pharmacy and central sterile supply services; minimum of one year experience in hospital pharmacy required. Salary open. Write P. O.-17, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

CHIEF PHARMACIST—To assume full charge of the department; 340-bed hospital; located in New York State. Experience in hospital pharmacy necessary. Salary open. Write P. O.-20, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington 7, D. C.

PHARMACIST—162-bed hospital located in Ohio; assume complete charge of the department; prefer woman with hospital pharmacy internship. Salary open. Write P. O.-21, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washingson 7, D. C.

ASSISTANT CHIEF PHARMACIST—185-bed hospital; prefer member of Seventh Day Adventist Church; write P. O.-22, Division of Hospital Pharmacy, 2215 Constitution Ave., N. W., Washington 7, D. C.

ASSISTANT TO CHIEF PHARMACIST—registered. 220-bed hospital presently expanding to 320 beds. Good personnel policies and salary, with regular increments. Write PO-18, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington, 7, D. C.

STAFF PHARMACIST—eligible for licensure in Connecticut; 279 bed hospital. New, modern general hospital located on Long Island Sound, only 28 miles from New York City. Excellent working conditions and personnel policies. Write PO-23, Division of Hospital Pharmacy, 2215 Constitution Avenue, Washington, 7, D. C.

CHIEF PHARMACIST—General 321 bed hospital. To assume complete charge of pharmacy and, ultimately, a central supply service. Require top-notch pharmacist, preferably with M. S. degree. Salary, $6,000.00. Write PO-24, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D. C.

CHIEF PHARMACIST—To establish new pharmacy department in 100-bed general hospital. Prefer applicant with two years' experience in hospital pharmacy or Master's degree. Salary, open. 40-hour week; two-week vacation. Write PO-25, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D. C.

CHIEF PHARMACIST—Kentucky registration required. Salary, $6,420.00; 40-hour week; four-week vacation; non-contributory retirement plan; guaranteed annual salary increases. Write PO 26, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D. C.

STAFF PHARMACIST—female preferred; 274 bed general hospital and 172 bed maternity hospital. California registration required. Salary, $525.00 per month; benefit program represents 17% of base salary. Write PO 27, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D. C.

CHIEF PHARMACIST—169 bed general hospital. South Carolina registration required. Salary, $300-400 per month. Write PO 28, Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, 7, D. C.

ASSISTANT CHIEF PHARMACIST AND STAFF PHARMACIST—550 bed general hospital in South Carolina; hospital experience preferred; salary, open; 44-hour week; two-week vacation. Write PO 29, Division of Hospital Pharmacy, 2215 Constitution Avenue. N. W., Washington, 7, D. C.

DIRECTOR OF PHARMACY—605 bed hospital located in the East; plan, organize and direct complete pharmaceutical service for this teaching hospital. Salary, $6,000.00 to $7,200.00. Write PO 30, Division of Hospital Pharmacy, 2215 Constitution Avenue, N. W., Washington, 7, D. C.

Inquires regarding positions in hospital pharmacy may be addressed to The Division of Hospital Pharmacy, American Pharmaceutical Association, 2215 Constitution Ave., N.W., Washington, D. C.

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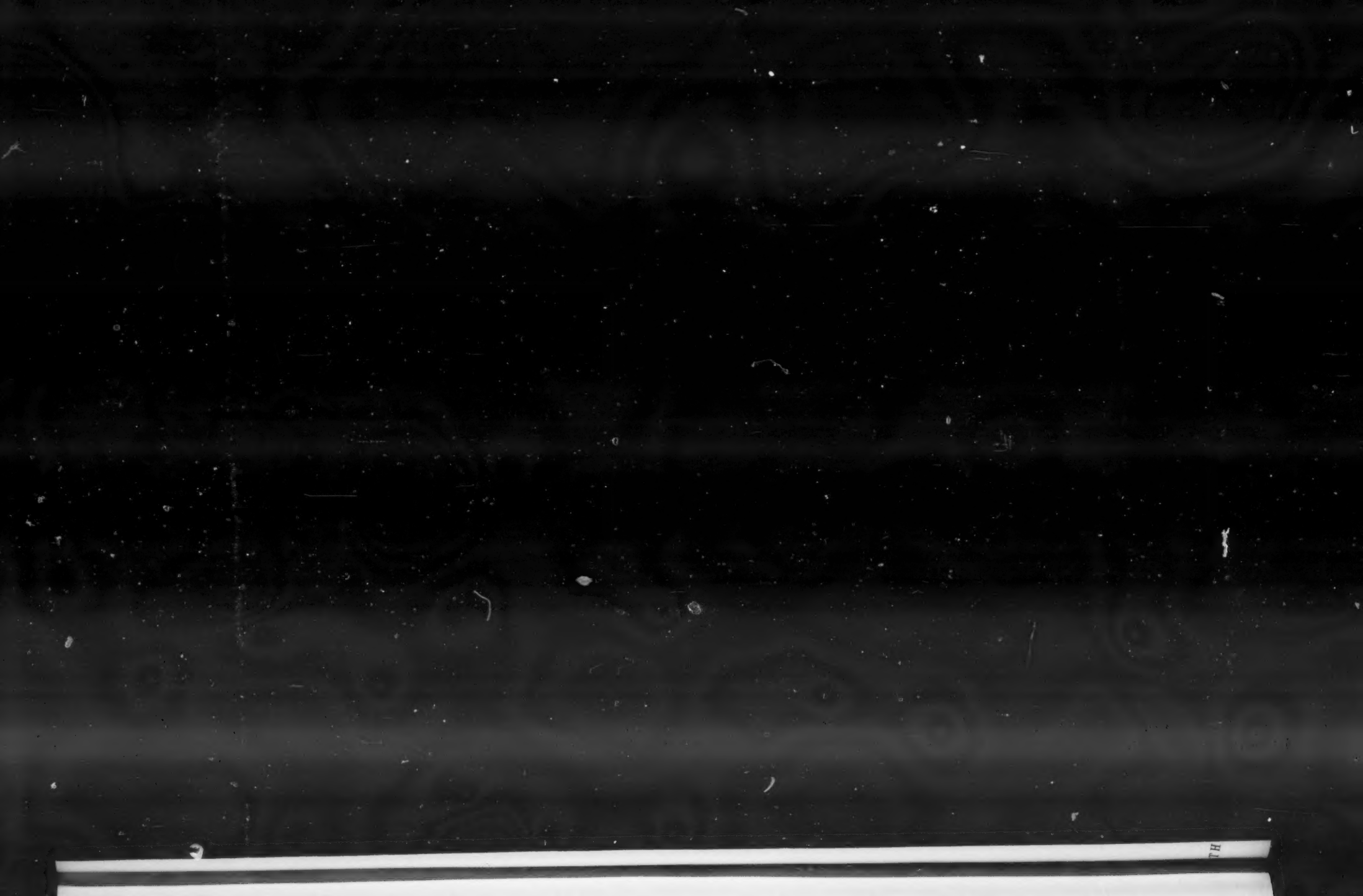

The BULLETIN

American Society of Hospital Pharmacists

INDUSTRY AND HOSPITAL PHARMACY
relationship between

APPLYING WORK SIMPLIFICATION
to hospital pharmacy

DISPOSABLE NEEDLES AND SYRINGES
current status

INTERNSHIP OBJECTIVES
for hospital pharmacy

ANNUAL INDEX
for 1957

VOLUME 14 NUMBER 6 NOV-DEC 1957

quiets an agitated cough reflex

•SYRUP

DOLOPHINE

HYDROCHLORIDE (Methadone Hydrochloride, Lilly)

. . . more effective in smaller doses than opium derivatives

Palatable Syrup 'Dolophine Hydrochloride' has proved extremely effective for suppressing cough in tuberculosis, bronchiectasis, bronchiogenic carcinoma, pertussis, and chronic congestive heart failure. Cough control extends over four to six hours or longer without altering respiratory rate or air volume.

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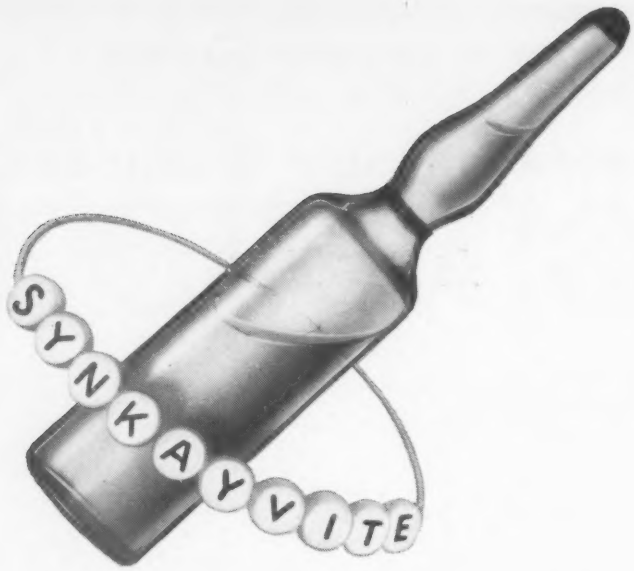

Newly born for the Newborn

Recent clinical reports (J.A.M.A. *164*:1331, July 20, 1957) have stressed the adequacy of low doses of water-soluble vitamin K analogs for infants and especially the undesirability of excess dosage in prematures. So you will be glad to know of these two new dosage forms of Synkayvite:

Ampuls, ½ cc, 1 mg, boxes of 12 and 100
Ampuls, ½ cc, 2.5 mg, boxes of 12 and 100

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Ampuls, 1 cc, 5 mg, boxes of 6, 25 and 100
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Ampuls, 2 cc, 75 mg, boxes of 6 and 25

Synkayvite administered routinely to the mother before delivery, or to the infant, is valuable, low-cost insurance against neonatal hemorrhage.

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Synkayvite is now available in convenient, color-break ampuls providing a full range of choice in dosage, according to the needs of prematures, full-term infants, older children and adults.

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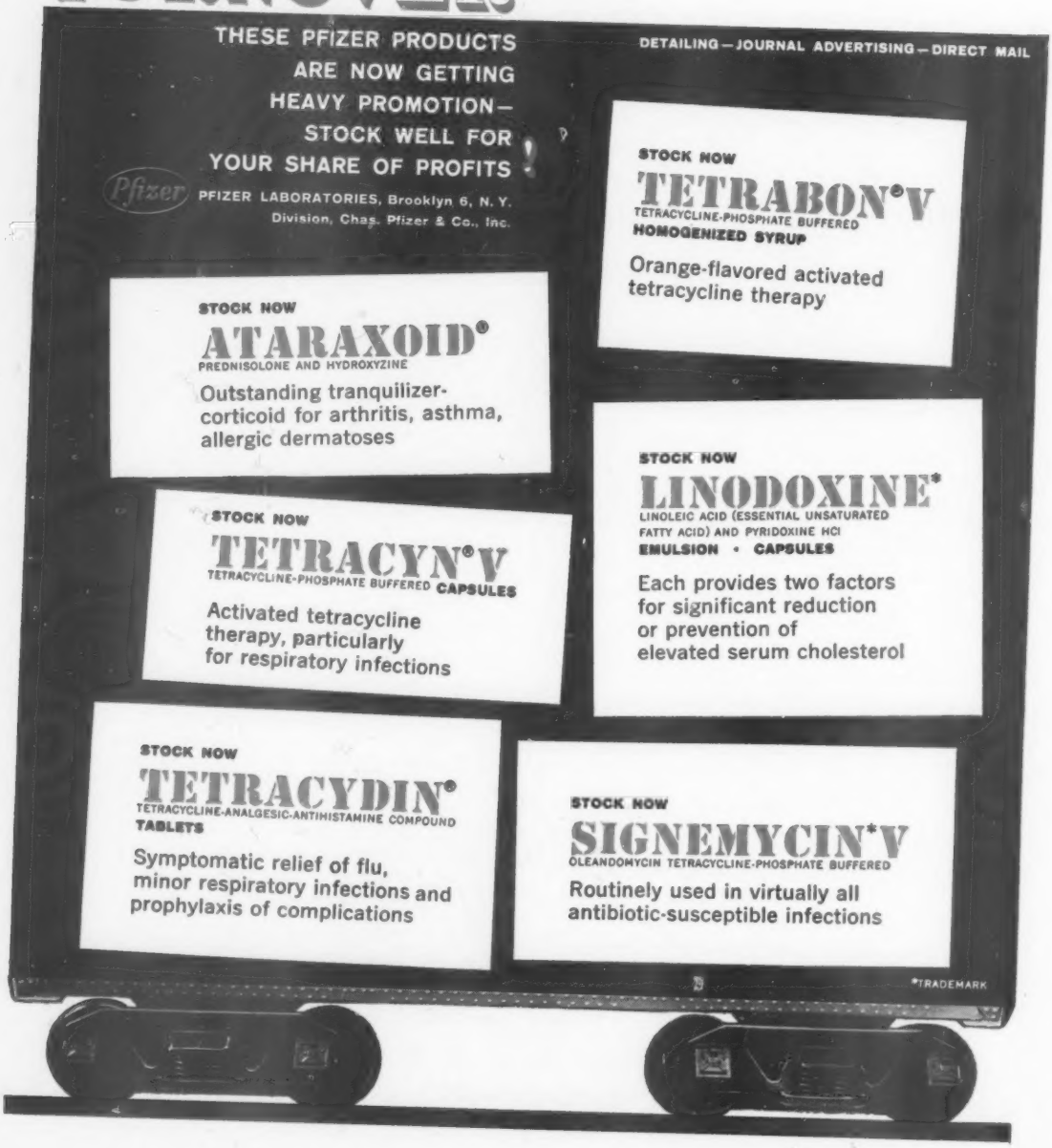

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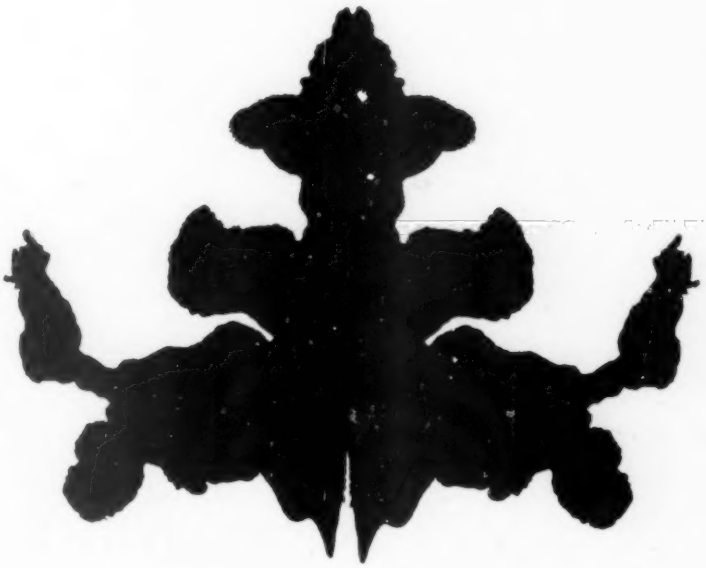
schizophrenia • manic states • psychoses associated with organic brain disease



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In extensive clinical experience—singularly free from toxicity

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- Photosensitivity—rare
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- Convulsions—not observed

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Tablets of 10, 25 and 50 mg.

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Enhanced potency with far less sedative effect

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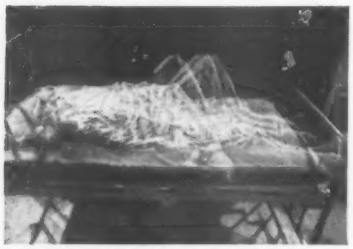
SQUIBB *Squibb Quality—the Priceless Ingredient*

sleep for the sleepless*



*The stroboscopic photo shows movements of restless sleeper (28-year-old male) after placebo. The following night the same patient was given nonbarbiturate Doriden 0.5 Gm. at bedtime. The result was an approximate 50 per cent reduction in overt motion and restlessness. Doriden® (glutethimide CIBA) acts within 15 to 30 minutes; induces 4 to 8 hours of sound, natural sleep; rarely causes morning hangover. **C I B A** Summit, N. J.

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